Exercise and Cancer Recovery

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Abstract

Disease and cancer treatment-related side effects such as decreased energy level, muscle weakness, and declines in functional status and body mass have been well documented. There is evidence that exercise, such as low intensity aerobics walking, Tai Chi, or cycling, results in an overall decrease in fatigue levels over the course of cancer treatment. Additionally, there is evidence that regular physical activity or exercise can decrease emotional stress, blood pressure, the duration of neutropenia, thrombocytopenia, and pain. Exercise also has been shown to increase quality of life and improve the maximal oxygen uptake during exertion, sleep patterns, and cognition. However, the majority of studies of exercise and cancer have been conducted with women with early stage breast cancer, limiting the generalizability of these studies to other cancer populations. The purpose of this systematic review is to provide a synthesis of the extant research evidence about the benefits of exercise related to cancer recovery.

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In recent years there has been a growing interest in the use of exercise as an intervention both during and after cancer treatment. Disease and cancer treatment-related side effects such as decreased energy level, muscle weakness, and declines in functional status and body mass have been well documented. Exercise regimens that prevent deconditioning and enhance strength and balance may provide an effective means of ameliorating the neuromuscular effects of treatment.

Exercise has also been used in the management of cancer-related symptoms, such as nausea, fatigue, pain, anxiety, and depression. Physical exercise has been demonstrated to improve body composition, enhance muscular endurance, flexibility, and quality of life (QOL). However, the majority of studies of exercise and cancer have been conducted with women with early stage breast cancer, limiting the generalizability of these studies to other cancer populations (Courneya, Friedenreich, Arthur, & Bobick, 1999). The purpose of this systematic review is to provide a synthesis of the extant research evidence about the benefits of exercise related to cancer recovery.

Search Strategy

Research evidence from 1986 through December, 2003 was located through searches of CINAHL (35 manuscripts) and MEDLINE (41 manuscripts). Key search terms were cancer, exercise, physical activity, aerobic exercise, and resistance exercise. Searches were limited to intervention studies of adults with cancer.

Cancer, Exercise, and Quality of Life

Quality of life (QOL) has been measured extensively in individuals with cancer. Four domains of quality of life have been proposed: physical well-being, psychological well-being, spiritual well-being, and social well-being (Ferrell, 1996). The cancer experience and cancer treatment have great potential to impact QOL. Individuals with cancer
have reported fatigue, depression, pain, anxiety, body image disturbance, loss of control, and social isolation resulting from cancer and its treatment. Although these effects tend to peak during treatment, they can persist for months or years.

Exercise has been used in the management of cancer-related symptoms, such as nausea, fatigue, pain, anxiety, and depression.

Several studies have found aerobic exercise enhanced quality of life (Courneya et al., 1999; Mock et al., 1994, 1997, 2001; Young-McCaughan et al., 2003). It has been proposed that exercise may enhance biopsychosocial mechanisms that underlie enhanced coping or self-efficacy, which in turn may alleviate or prevent the occurrence of some of the symptoms experienced, decreasing their impact on activities of daily living (Courneya, 2003). Kell, Bell, and Quinney (2001) found improved musculoskeletal fitness through resistance training and stretching is associated with enhanced health status and overall QOL. Physical exercise has been effective in promoting quality of life among cancer survivors. Courneya and Friedenrich (1997) examined quality of life in a retrospective study of 130 patients with colorectal cancer. Results indicated that individuals who maintained exercise regimens during diagnosis and treatment or returned to an exercise routine following treatment had overall higher quality of life than those cancer survivors who were inactive following treatment even though they had exercised regularly before the diagnosis. Quality of life issues such as weight gain, muscle atrophy, and fatigue related to cancer and its treatment have a physical basis and exercise regimens may address some of those specific issues. A recent review of 36 studies of cancer and quality of life found that aerobic exercise during or following cancer treatment resulted in improvements in quality of life, exercise capacity, flexibility, body composition, fatigue, and muscular endurance. Pain, nausea, diarrhea, sense of control, depression, self-esteem, and life satisfaction were also improved (Courneya, Mackey, & Jones, 2000).

Aerobic Exercise

Several randomized clinical trials using exercise training in individuals with cancer have been conducted (Cunningham et al., 1998; Decker, Turner-McGlade, & Fehr, 1989; Dimeo, Berta, Finke, Fetscher, & Mertelsmann, 1996; Dimeo, Fetscher, Lange, Mertelsmann, & Keul, 1997; Dimeo, Stiegitz, Novelli-Fischer, Fetscher, & Keul, 1999; MacVicar, Winningham, & Nickel, 1989; Mock et al., 1994, 1997; Nieman et al., 1995; Pfaehler, 1990; Segar et al., 1998; Winningham, 1983; Winningham & MacVicar, 1988; Winningham, MacVicar, Bondoc, Anderson, & Minton, 1989). With one exception, all studies used an aerobic exercise intervention in the form of walking or cycling. Of the eighteen studies reviewed, twelve studies focused exclusively on women with early stage breast cancer, and six studies used subjects with hematological malignancies.

The outcome measures examined by studies of exercise in cancer patients were primarily physical functioning (6 and 12-minute walk tests, cycle, and treadmill tests) and symptoms such as nausea, depression, anxiety, sleep disturbances, fatigue, and emotional distress. Several studies using supervised cycle ergometer exercise programs 3 times weekly for 10-12 weeks found that women with breast cancer who participated in the exercise program reported less somatization and nausea, increased functional capacity, and higher maximal oxygen uptake during exertion (VO2 max), decreased fat mass, and increased lean body mass as compared with the control groups (MacVicar et al., 1989; Segal et al., 2001; Winningham & MacVicar, 1988). Overall, the literature suggests that aerobic exercise following cancer diagnosis and even concurrent with treatment can have a positive effect on physical functioning and quality of life (Mock et al., 1994; Winningham, 1983). Aerobic exercise in the form of walking or cycling has also been used as an intervention to reduce fatigue and improve quality of life (Courneya & Friedenreich, 1997; Mock et al., 1997; Young-McCaughan & Sexton, 1991). The findings of these studies suggest that breast cancer survivors who engaged in regular exercise, such as walking, reported higher quality of life as compared to those who did not exercise.

Resistance Exercise

Numerous studies document the physiologic benefits of resistance or strength training in terms of increasing muscle mass, strength, and endurance (Brooks & Faulkner, 1988; Evans, 1996; La Forest, St. Pierre, Cry, & Gayton, 1990; Welle & Thornton, 1998). Following strength training, changes take place within the muscle to generate increased force. First, the cross-sectional area of the muscle increases in size (hypertrophy). Studies have demonstrated that this hypertrophy is the result of increased synthesis of actin and myosin, which make up the contractile element of the muscle resulting in reduced fatigability (Kraemer, Deschenes, & Fleck, 1988; Willems & Stauber, 2000). It is this accelerated rate of cellular protein synthesis in contracting muscles that increases muscle mass, and thus muscle strength (Al-Majid & McCarthy, 2001).

Secondly, studies of weight lifters following resistance training have inferred a type of neural learning or adaptation of the muscle that results in improved muscle activation following resistance training (de Lateur, 1994). In one study of muscle strength and physical functioning (Brill, Macera, Davis, Blair, & Gordon, 1999), it was determined that maintenance of muscular strength throughout the life span reduced the number of subsequent functional limitations.

Additionally, in studies of bone mineral density, muscle strength training stimulated increases in bone mineral...
Combination Exercise Regimens

Few studies have examined the effects of combinations of aerobic and resistance exercise in individuals with cancer. Nieman and colleagues (1995) examined the effect of a 60 minute supervised walking and weight training program for 12 breast cancer survivors. All women had completed cancer therapy within the last 4 years. Exercises were performed for 60 minutes 3 times weekly for 8 weeks. Physical and immune system functioning were measured by a treadmill test, 6 minute walk test, and natural killer cell activity measurement. The experimental group demonstrated increases in the 6 minute walk test, decreased heart rate, and improved leg strength. No differences between the intervention and control group were found in natural killer cell activity.

Another study of 20 breast cancer survivors (1-17 years post-diagnosis) who had undergone axillary node dissection and/or adjuvant treatment found no change in lymphedema following a program of 20-30 minutes of moderate intensity aerobic and resistance exercises performed 3 times weekly for 8 months (Harris & Niesen-Vertommen, 2000).

Exercise and Older Cancer Patients

The aging process is associated with documented declines in functional performance, loss of skeletal muscle mass (sarcopenia), loss of flexibility, muscle weakness, and decreased bone density (Courneya et al., 2004; Dutta, 1997; Hurley, & Roth, 2000; Tuli & Lyles, 2003). Cancer disease and treatment can further exacerbate these declines. Chemotherapy can contribute to muscular atrophy and declines in muscle strength (Bruera, Carraro, Roca, Barugel, & Chacon, 1986; Hollosy & Booth, 1976). Hormonal manipulation, often the treatment of choice in post-menopausal women with estrogen-dependent breast cancers, can cause arthralgias, myalgias, osteoporosis, and pathologic fractures (Meyer & Balducci, 2003). However, no studies have tested interventions aimed at exploring the appropriateness, efficacy, or safety of exercise in an older cancer population. Therefore, conclusions and recommendations regarding exercise in the older cancer patient must be extrapolated from older adults and cancer survivors in general. While many studies have been conducted testing the effects of exercise in individuals over 65 years of age, only a few studies will be highlighted here. In older adults, exercise has been shown to improve muscle mass and improve strength. In a study by Fisman and colleagues (1994), resistance training for 10 weeks without nutritional supplementation increased muscle strength by 90% in 87-year-old men and women. Strength training has been recommended as a preventative measure by age 50 as the loss of skeletal muscle corresponds to the loss of leg α-motor neurons at this age (Tseng, Marsh, Hamilton, & Booth, 1995). Fatouros and colleagues (2003) trained 78 year-old men (8 men per group) to a combined aerobic and strength training group, a cardiovascular training group, and a combination aerobic and strength training group. Participants in the exercise groups trained 3 times weekly for 16 weeks at 55-80% of 1 repeated maximum (1-RM) for resistance exercises and at 50-80% maximal heart rate for aerobic exercises. Weight, physical activity level and maximal oxygen uptake (VO2 max) were measured at baseline and the end of the training period. Muscle strength was measured at baseline, 8, and 16 weeks. There was no difference in VO2 max or body weight in any of the groups, but resistance exercises were shown to have a beneficial effect on joint range of motion and muscle strength.

A meta-analysis showed a beneficial effect of physical activity in the reduction of body fat that typically accompanied the aging process (Toth, Beckett, & Phehiman, 1999). While not limited to just older cancer patients, weight gain remains a common problem among women receiving adjuvant chemotherapy for breast cancer, and may negatively influence both upper and lower extremity muscle strength (Demark-Wahrfried, Riemer, & Winer, 1997; Demark-Wahrfried, Winer, & Riemer, 1993). Women treated for breast cancer have an average weight gain of 10 pounds that directly influences body composition (Demark-Wahrfried et al., 1993). Exercise programs have also been found to help improve functional status and the risk of falls in older persons (Gregg, Periera, & Caspertas, 2000; Spiridiso & Cronin, 2001).
In a subset analysis of two previously published aerobic exercise trials of post-menopausal breast cancer survivors, Courneya and colleagues (2004) found that older participants (> 60 years) may not have benefitted from the exercise training as much as their younger counterparts (< 60 years); but this analysis was limited by the relatively small sample size. Thus, while no published guidelines exist for older cancer patients regarding exercise, the American College of Sports Medicine and the National Institute on Aging have general, published guidelines of exercise recommendations in older adults. Older adults should participate in 30 minutes of moderate-intensity aerobic activity most days of the week. This includes such activities as walking, cycling, and swimming. Exercise intensity should start out low and progress slowly to the person’s ability and tolerance. Resistance or strength training exercises should be incorporated into the exercise plan to maintain muscle strength. Balance training consisting of lower body strengthening exercises of the hips and ankles is also recommended (American College of Sports Medicine Position Stand: Exercise and physical activity for older adults, 1998; National Institute on Aging, [n.d.]).

**Exercise and Conditions Related to Cancer and Cancer Treatment**

**Cancer-Related Fatigue**

Fatigue remains the most frequently reported symptom of individuals with cancer, and is experienced by the majority of individuals receiving treatment for cancer (Irwine, Vincent, Graydon, Bubela, & Thompson, 1994; King, Nal, Kreamer, Stroh, & Johnson, 1985). Fatigue has been described as lacking energy, feeling exhausted, being unable to concentrate, feeling lethargic and lacking motivation, and also as feelings of sleepiness, depression, and weakness (Winningham et al., 1994). The etiology of cancer-related fatigue is not fully understood and is related to disease and treatment factors (Visovsky & Schneider, 2003). Exercise has been shown to improve levels of fatigue experienced by patients with cancer. Winningham (1983) demonstrated the benefits of cycling exercise on physical functioning and locus of control in women undergoing treatment for breast cancer. Schwartz (1998) conducted a study of athletes who had cancer and found that exercise decreased the intensity, frequency, and duration of fatigue. In another study, Schwartz (2000) found that women with Stage II and III breast cancer who engaged in an 8-week, home-based, 15-30 minute aerobic exercise program 4 days a week had fewer days of severe fatigue and a pattern of decreasing levels of fatigue with each cycle of chemotherapy as compared to non-exercisers.

Cancer patient exercisers also reported a significantly improved quality of life compared to non-exercisers. Mock and colleagues (1994) studied the effects of a structured walking program for 14 women with early stage breast cancer who were receiving adjuvant treatment. The women who walked regularly adapted better to physical symptoms of chemotherapy, physical functioning, and psychosocial changes. They experienced consistent and progressive improvement during the course of chemotherapy, while the women who did not exercise got progressively weaker. In a more recent study Mock and colleagues (2001) found improved quality of life and physical functioning and significantly less fatigue and emotional distress in 52 women with Stage I, II or IIIa breast cancer receiving adjuvant chemotherapy or radiation who exercised at least 90 minutes 3 days a week. All five individuals experienced decreased fatigue and improved physical functioning over the six weeks of daily treadmill walking and were able to return to normal daily functioning without any significant limitations. A recent quasi-experimental study by Headley, Ownby, and John (2004) examined the effect of a seated exercise program on fatigue and QOL in 32 women with Stage IV breast cancer receiving chemotherapy. The women were randomized (16 per group) to either the intervention or control group. The intervention group performed a series of seated exercises 3 times weekly for four cycles of chemotherapy. Results indicated that the women participating in the seated exercise program had a slower decline in physical well-being and less fatigue as compared to the control group by the third cycle of chemotherapy.

**Cancer Treatment-Related Neuromuscular Toxicity**

Both radiation and chemotherapy exert effects that alter the sarcolemma, sarcoplasmic reticulum, and mitochondrial membranes leading to decreased ability of the muscle to generate force. Muscle weakness, imbalances, and impaired range of motion can occur. In women undergoing treatment with chemotherapy for breast cancer, lean body mass losses occur predominantly in the lower trunk and legs (Demark-Wahnefried, et al., 2001; Kutynec, McCargar, Barr, & Hislop, 1999). These larger muscles of the lower extremities are relied upon most for stability and activities of daily living. Thus, threats to functional health and safety result when these muscle groups become weakened. One study examined the effects of resistance exercise to prevent skeletal muscle atrophy in bone marrow transplant recipients receiving total parenteral nutrition (Cunningham et al., 1986). They found that while there appeared to be a muscle protein-sparing effect due to exercise, variations in baseline arm muscle area and nutrition protocols were confounding factors.
The incidence of peripheral neuropathy related to chemotherapy can be low to severe, depending on the agent used, the dose received, and age of the patient. Sensory neuron involvement produces the classic "stocking and glove" distribution of sensory loss in the extremities. Symptoms of neuropathy such as burning pain, numbness, tingling, and parenthesis can persist for months to years following treatment. Currently, there are no published trials that specifically examine the effects of either aerobic or resistance exercise programs specifically on cancer treatment-induced neurotoxicities. A trial is currently in progress by the authors testing the efficacy, feasibility, and acceptability of a home-based, resistance exercise intervention in women with Stage I - IIIA breast cancer who are receiving chemotherapy. Muscle strength, body composition, fatigue, and quality of life measures are being collected over the 12-week study period.

In recommending exercise regimens for patients with neuromuscular deficits, careful attention must be paid to issues of safety. Loss of sensation in the lower extremities poses the risk of falls and injury as the individual cannot sense changes in terrain while walking, and may have particular consequences for treadmill use. Loss of sensation also poses an increased risk of thermal and ischemic injury of the extremities as discrimination of hot or cold temperatures is impaired.

**Osteoporosis**

In general, the skeletal mass of physically active individuals is better than those who are sedentary. Resistance and aerobic exercises have demonstrated enhanced bone density in premenopausal women. Cross sectional studies of adults demonstrate that individuals performing weight-bearing exercise at > 60% of their aerobic capacity have consistently greater bone mineral density than non-exercisers. In post-menopausal women, loss of estrogen causes bone loss. Results of studies examining the effects of resistance and weight-bearing aerobic exercise in this age group show inconsistent results related to the maintenance or improvement in bone mineral density (Beck & Snow, 2003). While there is evidence that exercise can prevent osteoporotic fractures in older adults, the role of weight-bearing or resistance exercise in preventing fractures in individuals with cancer, particularly cancers that have the potential of metastasizing to the bone, is not known.

**Survivorship Recommendations for Exercise-Related Cancer Recovery**

There is a great deal of interest in the role of exercise as a rehabilitative strategy for cancer survivors, and this interest is expanding to include exercise as a preventative strategy for those undergoing cancer treatments. There is preliminary evidence to suggest that exercise is safe, feasible and beneficial for individuals with cancer. It must be noted, however, that the majority of evidence has been garnered from studies of women with early stage breast cancer, and these findings cannot be extrapolated to cancers at any site or stage. It is important that future research use rigorous, randomized clinical trial methods to generalize such findings.

Research concerning physical activity and/or exercise for cancer patients has largely focused on women with early stage breast cancer. Thus, these findings, too, cannot be generalized to other cancer diagnoses or stages. Additional research is needed to test the effects of increased physical activity and exercise on patients with different diagnoses and stages of disease. There is also limited data concerning the effectiveness of resistance exercise and/or combinations of aerobic and resistance exercise regimens on physical or psychological outcomes. However, the American Cancer Society recommends that physical activity and exercise instruction be included as a component of comprehensive cancer care. A study by Jones and Courneya (2002) of 311 cancer survivors found that 82% of the participants felt that their oncologist should initiate discussion of exercise and physical activity as part of the oncology consultation. Fifteen percent felt that the cancer survivor should initiate the discussion. The investigators concluded that exercise should be recommended both during and after treatment to patients with early-stage cancer. Women with breast cancer often gain as much as 5.5-13.6 pounds during adjuvant chemotherapy (Demark-Wahnefried, et al, 1993). Schwartz (2000) and Winningham (1983) found that exercise can assist women with breast cancer in maintaining body weight and reduce body fat mass while receiving adjuvant therapy. Therefore, education concerning activity and exercise should be included as part of routine health care for cancer patients. Women with breast cancer should also undergo clinical assessment of weight in addition to information concerning exercise.

The American Cancer Society recommends that adults should adopt a physically active lifestyle that consists of moderate physical activity for at least 30 minutes 5 days per week. Studies have shown that engaging in vigorous
activity on 5 or more days per week may further reduce risk of breast/colon cancer, and may forestall certain cancers and chronic illnesses such as obesity, heart disease, and diabetes (McTiernan, 2000; Slattery, Edwards, & Ma, 1997). Many studies have concluded that with exercise, such as low intensity aerobics walking, Tai Chi, or cycling, there was an overall decrease in fatigue levels over the course of cancer treatment (MacVicar et al., 1989; Mock, 1994, 1997, 2001; Schwartz, 1998, 2000). Additionally, there is evidence that regular physical activity or exercise can decrease emotional stress, blood pressure, the duration of neutropenia, thrombocytopenia, and pain. Exercise has also been shown to increase quality of life, improve V02 Max, sleep patterns, and cognition (Courneya et al., 2003; Dimeo et al., 1997, 1999; Hayes, Davies, Parker, Bashford, 2003; MacVicar et al., 1989; Schwartz et al., 2002; Young-McCaughn et al., 2003). At this time, there is no clear evidence regarding the effects of exercise on cancer treatment. It is recommended that individuals who are already engaged in an exercise program continue their activities as much as possible. Sedentary patients should start an exercise program slowly, beginning with stretching activities and short walks. It may be prudent to do lower intensity exercises while undergoing treatment, and build up slowly to more intense activity.

A few studies examined the effects of upper body exercises on lymphedema. Upper body exercises (swimming, resistance) are not contraindicated and concerns about vigorous upper body exercises increasing lymphedema appear to be unfounded. However, patients are advised to wear a compression sleeve during upper body exercises.

In summary, exercise appears to be a safe, feasible intervention that can have a positive effect in ameliorating many symptoms associated with cancer and its treatment. Discussions about strategies to assist patients in maintaining or increasing physical activity during or following cancer treatment should be a part of routine care.

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Connie Visovsky received her Bachelors and Master’s degrees in Nursing from the University of Rochester in Rochester, N.Y. She received her PhD from Case Western Reserve University in Cleveland, Ohio. Her program of research is focused on the neurotoxic and myotoxic effects of chemotherapy and biotherapy on individuals undergoing cancer treatment. She has an interest in resistance exercise as a means of ameliorating these effects. She is currently an Assistant Professor and National Cancer Institute Translational Oncology Research Post-Doctoral Fellow at Case Western Reserve University. In addition, Dr. Visovsky also maintains an active practice as an acute care nurse practitioner at University Hospital of Cleveland’s Ireland Cancer Center.

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