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WAITING FOR A CURE: BALANCING MEDICINE AND QUALITY OF LIFE FOR PEOPLE LIVING WITH CANCER

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INTRODUCTION

Cancer is a very complex disease, which our society has been unable to eradicate. The fact that we have been unsuccessful in finding a cure for cancer is not surprising given that this disease has been evolving and changing since it was first described in Egypt in 1600 B.C. (American Cancer Society 2009). Cancer is characterized by abnormal cell division resulting in invasion of tissues and tumour growth (National Cancer Institute 2010). Today over 100 types of this ancient disease exist (National Cancer Institute 2010). In Nova Scotia 6000 new cases were expected in 2009 (Canadian Cancer Society's Steering Committee 2009). It is estimated that 171,000 new cases of cancer were identified across Canada last year (Canadian Cancer Society's Steering Committee 2009). This translates to approximately 470 Canadians being told each day that they have cancer (Canadian Cancer Society's Steering Committee 2009). Imagine how that moment changes a life forever.

Once the diagnosis of cancer is confirmed, patients usually follow various daily, weekly, or monthly regimens of radiation therapy, chemotherapy, or other drug therapies. Whether these measures are for curative or palliative purposes, the side effects can be both physically and mentally debilitating. Once treatment is completed, and even during treatment, many patients find themselves looking for direction on how to improve their overall health. There is a large amount of research supporting exercise as a means of addressing both the effects of cancers and adverse effects of cancer treatment (Courneya & Friedenreich 2007, Galvão and Newton 2005, Hayes *et al.* 2009). From my perspective as a researcher and physiotherapist, we are not doing enough to ensure that cancer survivors are aware of the benefits of exercise and more importantly are participating in a regular exercise program. Although we may not have a cure for this disease, all cancer survivors should be well informed of the fact that exercise could improve their quality

of life (QOL) while they are living with cancer. In addition to this valuable knowledge is the early research showing that exercise may prevent cancer recurrence in some cases (Courneya *et al.* 2004). This paper discusses how exercise may prove to be the key to balancing medical or radiation cancer treatments and QOL. It also summarizes the various mechanisms behind these ideas and presents the many positive reasons why people with cancer should engage in exercise programs.

WHAT IS QUALITY OF LIFE?

Quality of life is defined differently across the health care literature (Hacker 2009). It is clear that QOL is a multidimensional concept that includes all aspects of a person's life (Hacker 2009). The University of Toronto QOL Research Unit explains QOL with the use of a conceptual framework (*Quality of life concepts* 2009). They state that QOL is "The degree to which a person enjoys the important possibilities of his or her life" (*Quality of life concepts* 2009). There are three domains with three sub-domains, each including being (physical, psychological, spiritual), belonging (physical, social, community), and becoming (practical, leisure, growth) (*Quality of life concepts* 2009). It is easy to understand how cancer could cause a sharp decline in QOL for some people. Many factors play into this change in QOL, but Visser and Smets (1998) concluded that QOL for cancer survivors is mainly predicted by fatigue and depression. Dagnelie *et al.* (2007) highlight the impact of fatigue on QOL for patients with breast or lung cancer undergoing radiotherapy. They found a high correlation between fatigue and overall QOL ($r = -0.76$; $P < 0.001$), concluding that patient-perceived fatigue is the primary factor in QOL (Dagnelie *et al.* 2007). A large group of Chinese women with breast cancer being treated with radiotherapy or chemotherapy reported a "cluster" of symptoms including mainly fatigue and pain, but also depression and anxiety (So *et al.* 2009). The authors found significant correlations among these symptoms which all resulted in negative changes in QOL (So *et al.* 2009).

The best way to measure QOL is to ask for the individual's perspective as they are the most appropriate to judge their own QOL (Hacker 2009). There are several valid and reliable outcome measures available for examining QOL in patients with cancer. Unfortunately these tools are not used regularly to screen patients with cancer for changes in QOL. Complete treatment of any cancer patient should include assessment of the various domains of their QOL. This information can guide the decision-making process for adjunct therapies, possibly identifying the need for regular physical activity (PA) when appropriate.

THE BENEFITS OF EXERCISE FOR CANCER SURVIVORS

The evidence continues to grow showing that exercise is beneficial in preventing cancer and improving the health status of cancer survivors (Courneya and Friedenreich 2007, De Backer *et al.* 2009, Galvão and Newton 2005, Hayes *et al.* 2009). Although the symptoms of cancer and the side effects of treatment vary greatly among patients, exercise is considered to be an advantageous adjunct therapy during and after medical treatment or radiation (Mustian *et al.* 2009).

Fatigue is one common complaint from cancer survivors which is often debilitating enough to cause problems in physical performance while inducing feelings of depression and anxiety and negatively impacting QOL (Dimeo 2001). Recent reviews on the effects of exercise in breast cancer survivors suggest that exercise enhances physical functioning, may mitigate fatigue, and improves QOL (Bicego *et al.* 2009, Markes *et al.* 2006, McNeely *et al.* 2006). Management of fatigue for breast cancer survivors may be as simple as 90 minutes of walking on three or more days per week (Mock *et al.* 2001). Last year, Chen *et al.* (2009) released results from a study which included 1,829 breast cancer survivors. At 36 months post-diagnosis they found that non-regular exercisers had lower QOL scores compared to those who exercised regularly at high intensities (Chen *et al.* 2009). The women in this study reported noticeable positive changes in physical, psychological and social well-being (Chen *et al.* 2009). Similarly, another group of sedentary breast cancer survivors, notably older women, reported worse moods and lower self esteem when compared to regular exercisers (Pinto and Trunzo 2004).

In 2003, Courneya *et al.* concluded that postmenopausal breast cancer survivors benefited from a 15 week exercise training protocol with dramatic improvements observed in QOL ($P = 0.001$), fatigue ($P = 0.006$) and aerobic capacity ($P < 0.001$) (Courneya *et al.* 2003). Another study had an even shorter training time of 12 weeks, combining both aerobic and strengthening exercises. These participants also reported substantial boosts in health-related outcomes and breast cancer specific QOL (Milne *et al.* 2008). A unique 2007 study distributed print materials about physical activity along with step pedometers (Vallance *et al.* 2007). They found that breast cancer survivors increased their physical activity by almost 90 minutes per week (Vallance *et al.*, 2007). This increase in activity resulted in lower fatigue levels ($P = 0.052$) and higher QOL scores ($P = 0.003$) (Vallance *et al.* 2007).

Yoga is becoming more popular with the general public and with breast cancer survivors. Studies have shown that yoga is ef-

fective in enhancing emotional outcomes and reducing fatigue in patients with cancer (Danahauer *et al.* 2009, Vadiraja *et al.* 2009). It is thought that the combination of exercise, improved breathing awareness, and the associated sense of relaxation are contributing factors in explaining how yoga improves QOL (DiStasio 2008). One encouraging study showed that this complementary therapy could significantly reduce chemotherapy-induced nausea and emesis ($P \leq 0.05$) as well as improve feelings of depression, anxiety and distress (Raghavendra *et al.* 2007). Twelve weeks of yoga proved to be beneficial when compared to the waitlist control group and resulted in an improvement in overall QOL ($P < 0.008$) and emotional well-being ($P < 0.015$) among a multi-ethnic group of breast cancer survivors (Moadel *et al.* 2007).

Echoing the results from breast cancer research, studies involving prostate cancer survivors have concluded that exercise positively impacts various areas of life including physical function, muscular fitness, HRQOL and fatigue (Thorsen *et al.* 2008). A pioneer study examined the effects of exercise in men with prostate cancer specifically undergoing androgen deprivation therapy (ADT) (Segal *et al.* 2003). The men who completed 12 weeks of resistance training reported higher QOL scores ($P = 0.001$) and less fatigue when performing activities of daily living ($P = 0.001$) compared to the men in the usual care group who did not partake in any exercise programs (Segal *et al.* 2003). Four years later Galvão *et al.* (2007) released a review of the three existing studies on the topic of ADT and exercise which all showed positive results in subjective and objective tests. It prompted the researchers to recommend that men on ADT should participate in regular strengthening and aerobic exercise regimens to reduce the many side effects associated with this treatment (Galvão *et al.* 2007). Another study involving men receiving radiation therapy with or without ADT found that resistance training and perhaps aerobic training reduce fatigue (Segal *et al.* 2009). Resistance training may also improve overall QOL ($P = 0.015$) and other health outcomes such as percent body fat ($P = 0.049$) and triglyceride levels ($P = 0.036$) (Segal *et al.* 2009). The most recent study released involving PCa survivors had 57 patients who were undergoing ADT participating in a combined aerobic and resistance exercise program for 12 weeks. Of interest here is the reduction in feelings of fatigue ($P = 0.021$) and some domains of QOL including general health ($P = 0.022$) and vitality ($P = 0.019$) (Galvão *et al.* 2010).

Exercise studies involving colorectal and bladder cancer survivors are also hopeful. A questionnaire completed by colorectal cancer survivors revealed that those who met public health exercise guidelines reported increased QOL and reduced fatigue

compared to those who do not meet these guidelines (Peddle *et al.* 2008). Meeting the minimum standard was defined as 60 minutes of strenuous intensity exercise or 150 minutes of moderate to strenuous intensity exercise per week (Peddle *et al.* 2008). A 2003 randomized trial compared QOL in those participants who decreased PA versus those who increased PA compared to baseline reports (Courneya *et al.* 2003). A significant difference in QOL was observed on the Functional Assessment of Cancer Therapy-colorectal scale (a cancer-specific QOL questionnaire) between these two groups in favour of those who increased PA ($P = 0.038$) (Courneya *et al.* 2003). Additionally, a population-based study of bladder cancer survivors concluded there that there is a linear association between meeting recommended PA guidelines and QOL (Karvinen *et al.* 2007). When compared to sedentary survivors, those who exercised showed positive changes in cancer-specific QOL ($P = 0.001$), bladder cancer specific QOL ($P < 0.001$), and various fatigue scales ($P < 0.05$) (Karvinen *et al.* 2007).

Some researchers suggest that an overall lifestyle modification such as a low fat diet, high fruit and vegetable consumption and PA are all needed to observe meaningful changes in QOL (Blanchard *et al.* 2004, Demark-Wahnefried *et al.* 2004, Doyle *et al.* 2006). Blanchard *et al.* found that patients with cancer who met more than one lifestyle modification recommendations (i.e. smoking cessation, physical activity) had significant increases in health related QOL (Blanchard *et al.* 2004). However, it is demonstrated here that there are several beneficial physical and mental effects, including domains of QOL, observed with various types of exercise such as aerobic, resistance, yoga, and combined programs. Interestingly, a systematic review published earlier this year concluded that high levels of physical activity can even reduce a cancer survivor's risk for mortality, or put another way, their quantity of life (Barbaric *et al.* 2010).

ANOTHER WORD ON MENTAL HEALTH

The risk and prevalence of depression increase with physical inactivity (aan het Rot *et al.* 2009). Therefore, physical activity can be especially vital in managing the overall care of patients with cancer who are at risk for or those with depression. However, depression can also affect someone's motivation to exercise (aan het Rot *et al.* 2009). Depression may actually lead to a sedentary lifestyle (Roshanaei-Moghaddam *et al.* 2009). Regular screening procedures for both depression and activity levels are pivotal in identifying those individuals who may need more direction and

supervision with exercise programs. Although there is evidence supporting exercise in the reduction of depressive and anxiety symptoms, there is a lack of knowledge translation in this area (Strohle 2009). This means that the information is current and available, but we are not telling our patients about it. A crucial action needed in some cases is interpretation of the data, proving that exercise decreases symptoms of depression (Mead *et al.* 2009). Although to some this might seem to be common knowledge, many people would not be aware of this relationship. Finally, the development of exercise programs for people with depression or anxiety may be warranted (Strohle 2009). Specific tactics such as an exercise journal, group-based activity sessions, or weekly check-ups may be needed to improve motivation and adherence.

WHY EXERCISE WORKS

Exercise improves both mental and physical health thereby improving one's overall QOL. This is true for everyone, not only cancer survivors. The beneficial effects of exercise on mood can be both psychological and physiological. Psychological changes are seen because of the distraction, self-efficacy and social interaction that can accompany regular physical activity routines (Peluso *et al.* 2005). The two most accepted physiological reasons for improvements in mood and QOL include changes in the neurotransmitters called monoamines and endogenous opioids called endorphins (Peluso *et al.* 2005). First, physical activity increases monoamine (i.e. serotonin, norepinephrine) transmission, which is similar to the response observed in patients taking anti-depressive medications (aan het Rot *et al.* 2009, Peluso & Guerra de Andrade 2005). These neurotransmitters are more available for synaptic uptake, which is believed to improve one's mood (aan het Rot *et al.* 2009). Second, endorphins are thought to be involved in the relationship between physical activity and mood through inhibition of the central nervous system via opioid receptors. Similar to the action of morphine, this inhibition results in a sense of calm and improved mood (Peluso and Guerra de Andrade 2005). Lastly, a third reason suggested is that exercise may be able to reduce abnormalities in the hypothalamic-pituitary-adrenal axis, which are observed in people with major depressive disorder (aan het Rot *et al.* 2009). In these individuals, cortisol and corticotrophin levels increase immediately following exercise resulting in overall stress reduction with long-term training (aan het Rot *et al.* 2009). Other factors may include alterations in neurotropic factors, changes in neurocircuitry, or presently unknown mechanisms (aan het Rot *et al.* 2009).

The exact cause of fatigue among cancer survivors is not known, but many explanations have been postulated (Dimeo 2001). Exercise can influence several of these factors (Dimeo 2001). Decreased oxygen transport and utilization caused by cancer treatments can be improved with exercise through higher concentrations of oxidative muscle enzymes (Dimeo 2001). Exercise can reverse the effects of prolonged bed rest during hospitalization including reduced muscle mass, plasma volume, and cardiac output (Dimeo 2001). Exercise may also reduce fatigue by facilitating neuromuscular efficiency as well as enhancing lung function (Dimeo 2001).

Obviously there are also other physical responses to exercise that would improve someone's QOL. In healthy individuals, it has been shown that 12 weeks of training can improve aerobic fitness (maximum oxygen uptake) as well as reduce depression and tensions scores (Annesi 2003). Bartholomew *et al.* (2005) reported that even acute bouts of aerobic exercise can increase physical well-being and vigour scores. It is also important to remember that patients with cancer are at risk for the same co-morbidities as people without cancer. It is well established that physical activity reduces cardiovascular disease risk through improvement of risk factors such as blood pressure, body mass index, and lipid levels (Mora *et al.* 2007). Whatever the reason, it would be easy to compile millions of testimonials from those with and without cancer supporting the claim that exercise has improved one or more aspects of their health and life.

MAKING IT A REALITY

There are many challenges in implementing and sustaining exercise programs for cancer survivors. Most importantly, infrastructure and leadership (*Roadblocks to cancer cures [editorial]* 2004) will be needed to enable future success in promoting physical activity and facilitating ways for cancer survivors to engage in regular exercise. Leadership implies both organizational and financial components (*Roadblocks to cancer cures [editorial]* 2004). From a financial standpoint, cancer is big business. This holds true for both the academic and clinical worlds. The cost of cancer care to Canadian tax payers in 2004 amounted to almost \$12 billion dollars (Canadian Cancer Society 2009). Operating costs of some Canadian research laboratories start at \$50,000 and can each be up to half million dollars in total (Canadian Cancer Society 2009). Although this seems like an ample amount of money to set-up and run exercise laboratories and programs for people with cancer, much of the funding for cancer research and treatment is awarded to those

working at the cellular or pharmacological levels. Oncologists, oncology nurses and family physicians are essential in ensuring that exercise is promoted among cancer survivors and that positions exist within our health care teams for exercise and rehabilitation specialists. Ideally, more time and money will be invested in programs that are focused on improving the health and well-being of cancer survivors through exercise.

HOW TO LIVE ACTIVELY WITH CANCER

Contrary to previous ideas on the management of cancer symptoms when patients were advised to rest in order to recover, we are now encouraging cancer survivors to participate in regular exercise programs (Lucia *et al.* 2003). This is especially true for overcoming feelings of fatigue (Lucia *et al.* 2003). Time constraints, lack of access to knowledge, and lack of motivation to start a program are three reasons that someone may not exercise. During these busy times, it may be helpful as clinicians to look at alternative ways to increase physical activity such as the 12 week telephone-based intervention described by Pinto *et al.* (Pinto *et al.* 2008). Researchers in this study made weekly phone calls to participants to encourage participation in bouts of moderate intensity physical activity (Pinto *et al.* 2008). The success of this type of intervention is evident at the 12 and 24 week follow-ups where participants reported enhanced QOL, decreased fatigue, and higher vigour (Pinto *et al.* 2008). This type of intervention is appealing because it is both convenient and cost-effective. To maintain interest in an exercise routine, a multidimensional rehabilitation program can be also used including activities such as individual exercises, sports, psycho-education, and information about exercise (van Weert *et al.* 2005).

It may be difficult to give specific exercise guidelines for cancer survivors to on a regular basis. Any number of scenarios could keep a cancer survivor from exercising, so patient “buy-in” on the positive effects of exercise is imperative. During or after treatment, there may be days when fatigue wins over exercise. Other days may be consumed by nausea and pain, and exercise is unthinkable. Also, depending on the cancer site, treatment and cancer stage, exercises may need to be targeted at certain body parts and avoided for others. Three components should be included in any exercise program: aerobic fitness, resistance training, and flexibility exercises (Courneya *et al.* 2004). The next step is to ensure that patients understand the proper techniques to the exercises that are being performed. Aim to complete low to moderate aerobic exercise, 3 to 5 times per week for at least 30 minutes. A full body strengthening

program, targeting a patient's weakest areas is suggested and is to be performed 2 to 3 times per week. Daily flexibility exercises are also recommended, especially for people who are beginning a new training program.

CONCLUSION

We should be positive about finding a cure for cancer, but we should also be focused more on the holistic treatment of cancer survivors, which involves more than just medicines and technology. Unfortunately in some cases, patients are given chemotherapy and radiation and sent on their way until their next check-up. Cancer survivors are generally faced many physical and emotional challenges over the course of their disease and these changes can significantly reduce a patient's QOL. There is an immediate need to address the physical and mental health problems that are common in cancer survivors. It seems to me that our focus as a health care team should be to find a balance between conventional cancer treatments and other treatments such as physical rehabilitation, lifestyle modification and psychological guidance. By doing this we can optimize the health of each cancer survivor now and in the future. The role of exercise in cancer management is an area of study worthy of receiving more attention from our professional and financial allies. With proper leadership and support, this information could be used to change the QOL of many people living with cancer.

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