EXERCISE IN CANCER RECOVERY: AN OVERVIEW OF THE EVIDENCE

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Abstract

With survival prospects following cancer diagnosis improving, more attention is being placed on the need for effective rehabilitation strategies. One strategy with the potential to positively influence the psychosocial as well as physical and functional status of patients with cancer is exercise. Increasing scientific evidence is available to support that participating in exercise during and following treatment for cancer, in particular breast cancer, is associated with improvements in psychosocial and physical outcomes. Although the exercise prescriptive characteristics have differed between investigations, the general recommended exercise prescription is of moderate-intensity, regular frequency (3-5 times/week) for 20-30 minutes per session. To ensure translation of research knowledge into clinical practice, future research must begin to evaluate how best to integrate exercise rehabilitation into the routine clinical care of cancer patients.

Cancer has become a leading cause of morbidity and mortality for Australians. However, while cancer is estimated to be responsible each year for about 261,000 years of life lost before the age of 75 years, survival prospects have never been better. Females have higher survival probabilities than males, with five-year relative survival rates being 63.4% and 56.8%, respectively.[1] For some of the more common forms of cancer, five-year survival prospects are even higher: melanoma, >90%; breast, >84%; prostate, >82%. Unfortunately, surviving cancer is not without its problems, as it is often associated with the presence of adverse physical and psychosocial side effects.

Treatment and side effects

Surgery, radiation therapy and systemic therapy (ie. drugs) represent the most common treatment modalities for cancer,[2] all of which have the potential to induce adverse patient effects. While the presence of side effects tends to peak during treatment, symptoms may persist for many months or even years following treatment.[3] Of all the potential physical and psychosocial side effects during and following cancer treatment, fatigue is regarded as one of the most common and disabling, occurring in 40-100% of patients.[4-6] As many as 40% of cancer survivors continue to report fatigue months or years following treatment,[7] with the presence of fatigue either significantly (31%) or somewhat (39%) adversely influencing survivors' daily lives.[8]

Increased survival rates after cancer treatment have placed more attention on the need for effective rehabilitative procedures. Arguably a public health imperative exists to assist this population to bridge the gap between treatment cessation and effectively returning to 'normal' daily lives. The role of pharmacological, behavioural and psychosocial interventions in this endeavour has been assessed.[9] Unfortunately, many of these are unlikely to address the physical and functional problems of patients with cancer.[10] Exercise is one strategy that has well-documented effects on all quality of life (QoL) domains with healthy adults,[11] as well as those with chronic disease,[12] including cardiovascular and pulmonary, metabolic, orthopaedic, neuromuscular and cognitive, emotional and sensory conditions. Hence it is a logical candidate for evaluation with cancer patients and cancer survivors.

Exercise and cancer

Exercise pre, during and post-treatment has been recommended for those with cancer since 1975, to prevent the sequelae of disuse and to maintain functional capacity.[13] However, only recently has there been sufficient evidence to support its effectiveness in reducing symptoms and improving QoL among cancer survivors.[3] The pioneering work in exercise and cancer recovery was first published in the early 1980s.[14-18] Since then the field has significantly expanded and now there are several reviews on the topic[2,3,19-26] highlighting that exercise is an important, safe, feasible and appropriate QoL intervention for cancer patients and survivors. What follows is a summary of this work.

Exercise interventions have focused predominantly on women with breast cancer,[27-32] although effects have been investigated with other patients including those with head and neck,[33] stomach,[34] colorectal[21] and prostate[35] cancers, melanoma,[36] cancer during childhood and adolescence,[37,38] as well as those undertaking bone marrow transplant treatment.[39,40] Observational (prospective,[40] retrospective[38] and cross-sectional[41] in design) and intervention studies[27,39,42,43] have been completed. Among the intervention studies, the effects of aerobic-based exercise have received the greatest attention. By far the most preferred exercise modes investigated include stationary cycling and walking. The potential benefits derived from resistance-based exercise programs have only relatively recently been studied.[44,45,35] Exercise intervention programs have been scheduled during[27,28,42,44] and/or following treatment,[37,45,46] implemented with varying degrees of supervision, lasting in duration from two[47] to 52[48] weeks, and studies have involved between five[45] to 442[49] participants. Exercise interventions usually included at least three exercise sessions per week of at least 15 minutes duration, at moderate intensities. However, these prescriptive characteristics vary across studies: frequency,

1-6 days/week; duration, 15-60 minutes/session; intensity, low to moderate (50-85% of maximal effort/heart rate). Finally, various physical and psychosocial outcomes have been assessed throughout these investigations.

Exercise and promotion of wellness

Usually the role of an exercise intervention during treatment is to minimise the adverse impact of the cancer treatment. Following treatment, rehabilitative interventions predominantly aim to reduce the physical and psychosocial burden of the disease and its associated treatment and to restore function and assist the return to 'normal' daily life. Examples of outcome measures assessed in exercise intervention studies among those with cancer include QoL, well-being, mental health, depression, anxiety, self-esteem, fatigue, fitness, nausea, cardiac function, body composition, immune function and haematology. These outcome measures can be broadly categorised as physical or psychosocial. Despite modest sample sizes in a large proportion of the studies, statistically significant beneficial effects have been observed.[3] Positive changes in physical measures, including fitness, flexibility, body composition, haematological parameters (such as natural killer cell cytotoxic activity, netropenia, thrombocytopenia, required platelet transfusions), fatigue and nausea, as well as physical and functional well-being, have been reported. Participating in physical activity during and following treatment has also been linked with: improved psychosocial status; increased vigour and coping behaviours; reduced depression, anger and anxiety; and improved QoL.

While another purpose of exercise interventions following treatment for cancer includes the prevention of secondary cancer and other chronic disease, to date this objective has largely been overlooked. Recently published findings from the Nurses' Health Study,[50] conducted in the US, has found that physical activity after a breast cancer diagnosis may reduce the risk of death from this disease, with the greatest benefits occurring in women who participated in the equivalent of walking 3-5 hours per week at an average pace. Compelling evidence is now available demonstrating that quality of survival is enhanced through exercise participation. Determining whether quantity of survival is influenced via exercise requires further investigation.

Exercise prescription – the clinical concerns

Clinical concerns regarding exercise prescription to cancer patients and survivors have included: the potential immunosuppressive effect of vigorous exercise; risk of bone fractures in those with compromised bone health; potential for elevating the cardiotoxic effects of cancer treatment; potential for exacerbating treatment side effects including fatigue, pain, lymphoedema, nausea; and the perceived reduction in the ability of cancer patients to tolerate exercise.[3] These clinical concerns have potentially dictated the prescriptive characteristics of the exercise interventions studied. Vigorous exercise has been avoided, as have high-impact types of activity. Furthermore, cancer survivors with particular side effects such as lymphoedema have until recently been excluded from participating in exercise intervention studies, with fear of exacerbating this condition the likely reason. While caution is appropriate when prescribing exercise to special populations, it is important to ensure that cancer survivors are not unnecessarily restricted from participating in activity types or intensities that would at worst do no physical harm, yet could lead to significant QoL improvements. For example, it makes sense that patients with bony metastasis avoid high-impact activities and/or activities that increase risk of falls. However, this same advice may not be appropriate for a woman who has completed treatment for breast cancer and enjoys the social and physical aspect of a game of netball. Exercise of vigorous intensity would be an inappropriate starting point for those whose functional capacity has significantly decreased following cancer treatment. However, there are likely cases (eg. cancer survivors who have been regularly active pre-diagnosis and remained active throughout treatment) for whom there are no physiological reasons why vigorous activity should be avoided. Furthermore, the concept of a standard exercise prescription for the group, individualised for each participant, needs to be understood. For example, for an exercise intervention of moderate intensity, one participant might run at a speed of 10km per hour while another walks at a pace of 20km per hour, yet both individuals will be working at moderate intensities.

Fatigue and lymphoedema merit special attention, as they represent cancer symptoms that have previously been treated with rest. It is now understood that exercise participation during and/or after cancer treatment at worst does not exacerbate fatigue.[4,40,45] It is also known that failure to participate in a progressive exercise program could potentially exacerbate fatigue rather than prevent or minimise it.[42] With rest, or when physical activity levels are down-regulated, a detrimental cycle of diminished activity which leads to being easily fatigued and vice versa is initiated. As for lymphoedema, evidence is accumulating demonstrating that participation in an exercise program does not increase lymphoedema risk or exacerbate the condition if already present.[44,48,53] Restricting the involvement in exercise of cancer survivors with secondary lymphoedema may limit their opportunity to participate in a potential rehabilitative strategy that could lead to significant changes in their physical and psychosocial well-being.

Importantly, among exercise interventions tested, now totalling more than 1000 patients diagnosed with various cancers and involving various treatment regimes, no major adverse events linked to exercise have been reported. There is sufficient evidence to support the notion that exercise is a safe, feasible and effective QoL intervention following cancer diagnosis.

Enhancing benefit and minimising risk

It is also important to clarify that exercise is 'safe' when being prescribed by appropriately qualified health professionals working in collaboration with treating specialists. Accredited exercise physiologists (accreditation from the Australian Association for Exercise and Sports Science) possess the necessary skills, experience and qualifications to undertake this prescription within the private setting. Furthermore, the effectiveness of exercise as a QoL intervention depends on the participant's motivation and adherence.[51] Although adherence rates

were not well-reported throughout exercise intervention studies, of those that were, rates ranged between 64-100%.[24] Compared with most physical activity interventions among healthy men and women where adherence rates are on average 50%, the rates for cancer survivors are high, potentially suggesting that cancer presents a 'teachable moment'.[52] The role of the physician must be acknowledged as a likely important factor influencing participants' motivation and adherence.[3] Courneya et al[3] summarises this issue by highlighting the results of international work demonstrating that at least 50% of breast cancer survivors reported that their physicians neither mentioned nor recommended exercise as part of their rehabilitation. Of the survivors who were recommended exercise, they participated in more physical activity than those who did not receive this information.

Exercise prescription recommendations

Table 1 presents the exercise prescription guidelines for early-stage cancer patients and cancer survivors. This table has been taken from a review by Courneya et al[3] published in 2000. Despite more work in the field since this was published, it continues to represent appropriate exercise prescription guidelines, with the possible exception of being too restrictive for mode. As indicated earlier, only recently has resistance exercise been included in exercise interventions under study. This is relatively surprising since a known role of resistance exercise is to increase muscle mass and to improve muscular endurance and/or attenuate muscle-wasting associated with various conditions, such as cancer. While there is much to be learned about the role of this exercise mode in cancer recovery, preliminary evidence suggests that resistance training alone or in combination with aerobic-based exercise has the potential to reduce fatigue and improve QoL.[35] Resistance exercise interventions tested have been of moderate intensity using large-muscle group exercises (eg. chest press, leg press); two sets, 8-12 repetitions of 60-70% of one repetition maximum[35,44] or one set to failure between 15-20 repetitions progressing to 8-12 repetitions.[53]

Future work needs to push the boundaries of this exercise prescription, so that we can begin to develop a better understanding of what constitutes optimal, desirable and necessary frequency, duration, intensities and type, and whether these levels are dependent on characteristics of the individual (eg. age, cancer type, treatment).

Translating evidence into clinical practice

Despite the high prevalence of physical and psychosocial impairment among cancer survivors, as well as the recognition that cancer rehabilitation is an essential component of cancer care, exercise rehabilitation does not yet form part of standard care. If patients have the inclination and knowledge, they may access resources available within the community to assist in their rehabilitative endeavours. These are somewhat limited, with more options currently available for breast cancer survivors. On a national front, Cancer Councils around Australia provide counselling services, information, support services and offer a 'living with cancer' education program. The YWCA's Encore program is also available for women with breast cancer and some hospitals may provide their own rehabilitative programs, such as the STRETCH or the domiciliary allied health acute care and rehabilitation service (DAART) programs for women undertaking breast cancer treatment. However, of the programs available for cancer survivors in Australia, few encompass components that address both the psychological as well as functional concerns.[54] Of those that do include some form of exercise, the prescriptive characteristics are likely to fall below what current research recommends and to focus on specific areas only rather than embracing a whole-body approach. For example, exercise programs tend to occur once per week

Table 1: *Exercise prescription guidelines for early-stage cancer patients and cancer survivors*

Parameter	Recommendation and comment
Mode	Most exercise involving large muscle groups is appropriate, but walking and cycling are especially recommended because they are safe and tolerable for patients. Exercises are modified based on acute or chronic treatment effects from surgery, chemotherapy and/or radiotherapy.
Frequency	At least 3-5x/wk, but daily exercise may be preferable for deconditioned patients who do lighter intensity and shorter duration exercises.
Intensity	Moderate, depending on current fitness level and medical treatments. Guidelines recommend 50-75% VO2 max or $HR_{reserve}$, 60-80% HR_{max}, or an RPE of 11-14. $HR_{reserve}$ is the best guideline if HR_{max} is estimated rather than measured.*
Duration	At least 20-30 minutes continuous exercise; deconditioned patients or those experiencing severe side effects of treatment may need to combine short bouts (eg. 3-5 minutes) with rest intervals.
Progression	Patients should meet frequency and duration goals before they increase intensity. Progression should be slower and more gradual for deconditioned patients or those who are experiencing severe side effects of treatment.

* $HR_{reserve}$ = maximal heart rate (HR_{max}) minus standing resting heart rate (HR_{rest}). Multiply $HR_{reserve}$ by 0.60 and 0.80. Add each of these values to HR_{rest} to obtain the target HR range. HR_{max} can be estimated as 220 minus age (years). HR = heart rate; RPE = rating of perceived exertion; VO2 max = maximal oxygen uptake.

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and to emphasise light intensities or to target shoulder and arm function. For those patients who have adequate financial resources, the services of an accredited exercise physiologist could be used to assist in their physical rehabilitative endeavours (Medicare rebates are now available for payment of these services). However, clearly this option is not an appropriate public health solution.

Conclusion

The quality of research on exercise and cancer varies, with few rigorous randomised control trials being completed. Difficulties in recruitment, overcoming the notion that patients during and after cancer treatment need to 'take it easy and rest' and yet at the same time avoid ethical implications of only providing a potential effective rehabilitative strategy to some participants, contribute to the flaws in study designs. However, other contributing factors include lack of measuring adherence, lack of quantification and control for pre-intervention activity levels, poor data collection of potential confounders and failure to use an intention-to-treat analysis. Cancer includes over 100 types and treatment strategies often vary both between and within cancer types, also contributing to the inconsistencies observed across exercise and cancer studies. Generally speaking, the quality of work in this area has gradually improved over the years. Nevertheless, more rigorous randomised control trials that are well described, involving larger sample sizes and population-based samples are required to continue to advance our understanding in this research arena. Furthermore, our understanding of how we can best assist cancer survivors to become active needs substantial improvement. Therefore, future work must address the feasibility and acceptability of various exercise programs from the perspective of the survivor as well as the medical profession. That is, how can exercise programs be feasibly integrated into the routine clinical care of people with cancer, for the purpose of minimising the impact of cancer treatment, restoring QoL following treatment and preventing recurrence and other chronic disease. □

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