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Is there a Correlation between Resistance Training and Cancer?

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Abstract. Although the importance of resistance training for a variety of health benefits has been recognized for quite some time, its effects on the risk of different types of cancer is not yet clear and additional research into this area has been recommended. Thus, in the present report we will summarize the most important updates on how exercising and especially resistance training could be or not correlated with the very complex cancer pathology. In this way, the recommendation for moderate to vigorous physical activity and resistance training are supported by the current level of knowledge in this area, which shows a reduction in risk of death from cancer as a result of increased cardiorespiratory fitness and muscular strength. In addition, the available data suggests that physical training programs have beneficial effects on the physical or psychosocial capacity of the cancer patients, with improved aerobic capacity, muscle strength and quality of life. Based on these findings, it seems that it could be recommended for the strength training to be incorporated for decreasing the risk of developing cancer, as well as for cancer rehabilitation, with careful screening of the patients and their supervises during training.

Keywords: cancer, exercising, resistance training.

Introduction

Cancer accounts for 23% of all deaths in the United States and is the second leading cause of death. In 2013 it was estimated that every year approximately 1.6 million new cancer cases would be diagnosed and 68% of survivors would live more than 5 years [1].

Moreover, the number of cancer survivors is expected to continue increasing each year with improvements in early detection and treatment. In addition, cancer treatment is often associated with many adverse physical side-effects including muscular atrophy, decreased muscle strength and reduced aerobic capacity [2]. These side-effects are known to contribute to the development of cancer-related fatigue [3]. It is also known that about 70% of cancer patients report fatigue complaints during chemotherapy and radiotherapy [4]. Furthermore, even years after the treatment, fatigue is found to still be a problem for up to 30% of cancer survivors and has a negative impact on the quality of life of the patients [5].

Unfortunately, most physicians are usually recommending rest or a reduction in the amount of physical activity as a “treatment” for fatigue [6]. This creates a physiological paradox because inactivity induces muscle catabolism, causing further deconditioning, which results in even more fatigue [7].

Thus, recently several studies examined the effect of physical activity in cancer survivors [2,8,9]. Overall, most data demonstrated that physical training programs had beneficial effects on the physical or psychosocial capacity of the cancer patients. For example, physical activity in cancer survivors has been shown to improve aerobic capacity, muscle strength, body composition, the quality of life or to reduce fatigue [10-12].

In this way, there are many lifestyle-related factors that are associated with cancer mortality. These factors include for example smoking or having a poor diet, since obesity also increases the risk of cancer [13-15]. In this context, another important lifestyle factor is the level of physical activity [16, 17].

In fact, the International Agency for Research on Cancer estimated in 2002 that up to one third of several types of cancers could be attributed to a sedentary lifestyle and excess of body fat [18]. A dose-response for exercising in general has been suggested. Even more, it has been found that engaging in longer exercise sessions or exercising at higher intensities or for more years is associated with a greater reduction in the risk of developing cancer [18].

Thus, recently increasing evidences are highlighting the beneficial effects of muscular strength in the prevention of chronic diseases [19]. In this way, resistance training is a major determinant of muscular strength and is currently recommended by the most influential health organizations, such as the American Heart Association and the American Cancer Society, for improving both general health and fitness [20-23].

Although the importance of resistance training for a range of health benefits has been recognized in recent physical activity guidelines [24-27], its effect on the risk of different types of cancer is not clear, and additional research into the effect of resistance training has been recommended [28]. In this aforementioned context, we will summarize here the most important updates on how exercising and especially resistance training could be or not correlated with the very complex and multifactorial general cancer pathology.

Resistance training and cancer risk

Mechanistically speaking, when it comes to the correlations between the resistance training and the risk of getting a certain type of cancer, it is quite accepted now that obesity is associated with increased risk of several cancer types, including colon, breast, endometrium, liver, kidney, esophagus, gastric, pancreatic, gallbladder, and leukemia and it can also lead to poorer treatment and increased cancer-related mortality [31]. Still, the biological mechanisms underlying the relationship between obesity and cancer are not well understood.

Adding that the prevalence of overweight and obesity exceeds 66% in the United States [32] or the fact that overweight and obese people are also at a substantially higher risk of disability [33] or death [34, 35], it seems that these results have important implications for public health.

Until recently, exercise recommendations to prevent or treat obesity have focused mainly on aerobic activities because cardiorespiratory training increases total energy expenditure, yet resistance exercise should be considered an important complement for body weight control, mainly because it increases the metabolically active muscle mass [36].

An increase in muscle mass results in any circumstances, and especially during physical inactivity, in a higher resting energy expenditure. The energy expenditure related to muscle metabolism is the only component of resting energy expenditure that might vary considerably [36]. Unlike muscle mass, the resting metabolic requirements of splanchnic tissues, brain, or skin do not vary under normal conditions, mainly because of their relatively constant mass and protein turnover rates. In contrast, significant variations in muscle mass are possible, and the rate of muscle protein turnover (synthesis and breakdown) may vary as well.

The synthesis and breakdown of muscle protein are principally responsible for the energy expenditure of resting muscle. In theory, every 10 kg difference in lean mass translates to a difference in energy expenditure of about 100 kcal daily, assuming a constant rate of protein turnover [36]. A difference in energy expenditure of about 100 kcal daily translates to approximately 4.7 kg of fat mass yearly. This means that over a long period of time the maintenance of a large muscle mass and consequent muscle protein turnover can contribute to the prevention of obesity. Therefore it is reasonable to presume that when sustained over time, resistance exercise training helps preventing or reverting increases in body fat [37].

For example, it appears biologically plausible that resistance training may reduce the risk of colon cancer, since resistance training has an effect on several biological mechanisms that are thought to be associated with the development of colon cancer, including insulin sensitivity and glucose uptake [28, 29]. Other possible mechanisms include improved immune function and lower exposure to systemic inflammation. Resistance training has also been shown to have beneficial effects in cancer patients, such as improved aerobic capacity, body composition and decreased fatigue [30]. Still, although there is convincing evidence that physical activity reduces colon cancer risk [38], the majority of research in this area has focused on aerobic activity, and to date, there is little published research about the effect of resistance training on the risk of colon and rectal cancers.

However, we did found one case control study of colorectal cancer in Western Australia in 2005–2007, on a total of 918 cases and 1,021 controls, which reported some initial evidences that resistance training may be inversely associated with colon cancer risk, independently of other recreational physical activity. In this way, in each of the age periods, as well as over the lifetime, performing resistance training was associated with a lower risk of colon cancer, although none of these results were statistically significant. As such, these results should be still treated with caution [39].

Also, in another study, Koffler and colleagues showed that resistance training accelerated whole bowel transit time by 56% and thus it could be plausible to assume that strength training might reduce the risk of colon cancer through this specific mechanism [40].

Resistance training during the treatment for cancer

As we previously mentioned, studies generally involving exercising in patients with cancer have focused more on aerobic exercise as an intervention [41-45]. These studies are indicating that aerobic exercise has beneficial effects on cardiovascular fitness, body composition, self-esteem, mood states, and fatigue, during treatment for a large variety of cancers [46-49].

Of course, it is known that resistance training requires the musculature of the body to move against some type of resistance [50]. In this way, it was demonstrated that in healthy older men, strength training elevates mood and helps to build muscle tissue and reduce body fat [51-57].

In this context, another inquiry will be also to found the level of training adaptation that will occur after a strength training adaptation on men with prostate cancer, which have of course have decreased levels of testosterone induced by androgen deprivation therapy, since testosterone levels are related to changes in muscular hypertrophy and gains in muscular fitness.

Moreover, healthy young males and females demonstrate an increase in testosterone levels after an acute resistance training session at 80% of one-repetition maximum (1-RM), and resting testosterone levels are increased in resistance training (80% of 1-RM) of middle-aged sedentary males [50].

There are also studies demonstrating the benefits of resistance exercise for improving symptoms of fatigue and health-related quality of life for example on 155 patients receiving androgen deprivation therapy for prostate cancer, when compared to the control group. Despite the low level of testosterone the authors also reported a significant increase in muscle strength, both in the upper body and lower body. Still, no significant effect was observed regarding the body composition and testosterone levels after the strength training intervention [58].

Thus, the aforementioned study clearly shows that resistance exercise improves symptoms of fatigue and health-related quality of life in men with prostate cancer receiving androgen deprivation therapy. More important is the fact that this is the first study to demonstrate that resistance exercise, rather than aerobic exercise, has a benefit of reducing the symptoms of fatigue related to cancer and its treatment

[44,49,59]. Even more, a three-point difference on the fatigue scale was observed in this study and the difference is similar, for example, to the magnitude of improvement observed in people receiving erythropoietin for the anaemia of cancer [60]. Thus, it seems that a progressive strength training program can be an important component of the supportive care for these patients.

Muscular strength and cancer mortality

In addition, the possible association between muscular strength and cancer mortality has been examined in several studies [61-64], but inconsistent results were found. A possible limitation of these studies may be the fact that they assessed muscular strength via a handgrip test, which provides information derived from only a small muscle group (e.g. the forearm).

Measuring the strength in additional muscle groups, especially in larger ones, should provide a more accurate result of the individual muscular strength. In addition, none of these studies accounted for cardiorespiratory fitness, which has been shown to be a strong predictor of cancer mortality [65-72]. One study has measured muscular strength in large muscle groups from both the upper and lower body. This study measured muscular strength in the upper and lower body using a strength testing protocol of variable resistance weight machines.

Upper body strength was assessed with a one repetition maximum supine bench press, and lower body strength was assessed with a one repetition maximum on a seated leg press.

In this way, the results of this study showed that muscle strength is inversely and independently associated with all-cause and cancer mortality in men, even after adjusting for cardiorespiratory fitness [30].

Resistance training for cancer survivors

With improvements in cancer diagnosis and treatment, the number of individuals living with cancer will continue to increase in forthcoming years. Thus, identifying factors that increase the quality of life and reduce all-cause mortality risk during cancer survival is of great importance [73-79].

As mentioned before, muscle atrophy results from a sedentary lifestyle and prolonged bed rest. As expected, muscle atrophy was found to be worsened in cancer patients by tumour factors and the side-effects of medication [80-82].

Fortunately, skeletal muscle has shown great adaptability with appropriate training stimuli even in cases of severe muscle atrophy and fatigue showed in cancer patients [80]. Also, progressive strength training has been shown numerous times to increase lean body mass, muscle protein mass and muscle strength. More so, it has been demonstrated that it improves physical function in healthy, both young and elderly subjects [83].

Therefore, strength training in cancer patients could prove to be an important physiological intervention for regaining the lost muscles and improving muscle quality and consequently improving the overall quality of life in cancer survivors [93].

In addition, we have found three studies that have investigated the outcome of strength training programs in cancer survivors [84-86]. However, two of these studies explored the strength training effect on cancer survivors during treatment, while only one study used strength training after treatment, conducted on a selected subgroup of prostate cancer patients receiving androgen deprivation therapy [84].

Moreover, the research regarding strength training in cancer survivors is limited, with the general recommendations about optimal intensity, frequency and duration of strength training lacking in most of the cases. For example, The American College of Sports Medicine (ACSM) proposes rather low to moderate exercise intensities [87].

Still, one study examined the potential benefit of strength-training at high intensity on cancer survivors [88]. This research, conducted on 57 patients (13 men, 44 women), had as a intervention a strength program consisted of six exercises targeting the large muscle groups as follows: 1) vertical row (focusing on longissimus, biceps brachii, rhomboideus); 2) leg press (quadriceps, glutei, gastrocnemius); 3) bench press (pectoralis major, triceps); 4) pull over (pectoralis, triceps brachii, deltoideus, trapezius); 5) abdominal crunch (rectus abdominis); 6) lunge (quadriceps, glutei, hamstrings). Firstly, strength exercises were performed at 65% to 80% of one-repetition maximum (1-RM) and consisted of two sets of 10 repetitions, followed by 35 to 40% of 1-RM but more (20) repetitions. Also, it is important to be mentioned that every 4 weeks the training progression was evaluated, and the training result was adjusted by means of a 1-RM test. The results showed that, although the training intensity was high, the program was well tolerated by all patients. In this way, only six patients dropped out of the program, not because of the high intensity, but rather considering the cancer recurrence or metastatis, while five patients dropped out because of other reasons.

Thus, we emphasize that none of the patients dropped out because the program was too intense, the result of this study showing significant improvements in muscle strength after training. The largest increase in muscle strength was observed in the first 8 to 12 weeks of training. These data are similar to the observations in healthy subjects and reflect the fact that the initial increase in muscular strength can be explained by an improved neuromuscular adaptation. In addition, the lunge and pull over exercises show the greatest increase. We also have to mention that these exercises are the ones in which substantial progress can be made by improved coordination along with an increase in strength.

Finally, this study demonstrates a significant improvement in muscle strength, maximal oxygen consumption and health-related quality of life after a high-intensity strength training program in cancer patients lasting 18 weeks. In addition, muscle strength was related to physical functioning before and after training. Based on these findings, it seems that it could be recommended to incorporate high-intensity strength training in cancer rehabilitation, with careful screening of patients and supervision during training.

In contrast, the American College of Sports Medicine proposes exercise intensities of 50% of 1-RM with 2-3 sets of 3-5 repetitions building to 10- 12 repetitions [87]. In this way, perhaps from a physiological point of view, these guidelines seem to be too low for an optimal training effect [89-90]. Still, a possible reason for why these guidelines regarding the intensity of strength training are so low is an unwillingness or moderation to expose these patients to risks and possible injuries at high intensities. Also, since cancer patients are undergoing intense psychological and physical stress, these guidelines perhaps recommend that patients should be treated with care and only do low intensity exercise.

This could be explained by the fact that in 2003, when the guidelines were formulated, research about strength training was very limited. Moreover, it has been shown in healthy subjects that improvements from a strength training program are more effective when heavier loads are used. Maximal muscle gains, maximal strength and the subsequent hypertrophy can only be achieved when utmost number of motor units is recruited and this happens with high training loads [89]. In addition, other tissues such as bone also respond more favourably to such heavy loading. This could also have a clinical relevance, since in post-menopausal breast cancer survivors, the bone mineral density is lower than normal, and it has been shown that strength training helps increasing it [97].

What is the optimal dose-response balance for the resistance training in cancer survivors?

A variety of studies have demonstrated that relatively short sessions of regular resistance training can increase muscle mass in adults of all ages, even through the 10th decade of life [91]. Some other studies have also demonstrated that the benefits of resistance training are more pronounced if exercises are muscle site specific, have a high intensity, and also when resistance training is combined with intake of calcium and vitamin D [92,93]. In fact, our research group also previously demonstrated that pre-administration of vitamin C could reduce the increased exercise-induced oxidative stress status in untrained subjects [94-96].

In addition, resistance training can provide functional benefits and improvements in overall health and well-being, including increased bone mineral density [97], improved physical performance [98], and cardiovascular health [99]. Consequently, resistance training may have beneficial effects in cancer patients in terms of reducing muscle wasting or help regaining lost muscle mass, as well as improving muscle function. This may lead to reduced fatigue levels and an overall enhancement in mental health, as our group previously described in various neuropsychiatric disorders [100-105].

Still, the optimal resistance training program for adult cancer survivors is yet to be established. Current exercise guidelines for cancer focuses more on the importance of participating in aerobic exercise, complemented with flexibility exercises and often makes no mention or a minimal one of resistance training [106,107].

Thus, considering that the dose–response relationship of resistance training for cancer patients has not yet been clarified, we lack clear recommendations for optimal intensity. Still, as mentioned above, findings from the literature support a full body routine as an appropriate training method to increase muscle strength in cancer patients and to improve body composition both in the short and the long-term. More so, full body routines are important for correcting potential muscular deficiencies often encountered in the cancer patients. The use of weights for upper body is mainly recommended to improve pain, disability, and range of shoulder movements in patients treated for breast or head and neck cancer.

Also, it seems that overall resistance training is well tolerated in adult cancer patients. We did not found any studies that reported significant adverse effects. Only one patient with head and neck cancer experienced an increase in pain as a result of soft-tissue injury to the scapular region due to resistance training [108]. The optimal frequency for resistance training appears to be 2 times per week. Also, the intensity of resistance training could play an important role in its benefits on cancer survivors.

In addition, a meta-analysis performed by Strasser et al. in 2013 suggested that strength training performed at low- to moderate-intensity at 75% of 1RM may promote equivalent gains in lean body mass and strength as moderate to high-intensity [109]. Furthermore, other studies concluded that low- to moderate-intensity resistance training is equally or even more effective at lowering percentage of body fat than is high intensity resistance training. In addition, the intensity should be such that fatigue results after 12–17 repetitions, corresponding to 60%–70% of 1RM [110]. Also, a minimum of two sets per muscle group, per week, should be performed at the beginning of the program and this should be progressively increased to a maximum of six sets per muscle group, per week. Thus, based on this analysis of dose–response evidence, there is little to suggest that a greater number of resistance training sets will lead to greater improvements in muscle function, body composition and fatigue in cancer survivors [109].

Conclusions

Thus, the available data clearly shows that it might be possible to reduce all cause mortality by promoting regular progressive resistance training two or three days a week, focusing mainly on the major muscle groups of the upper and lower body. Also, resistance training should be a complement rather than a replacement for aerobic exercise. In addition, the recommendation for moderate to vigorous physical activity and resistance training are supported by the current level of knowledge in this area, which shows a reduction in risk of death from all causes, including cancer, as a result of increased cardiorespiratory fitness and muscular strength. Based on these findings, it seems that it could be recommended for the strength training to be incorporated for decreasing the risk of developing cancer, as well as for cancer rehabilitation, with careful screening of patients and their supervise during training.

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