Role of physical activity in onset, prevention and treatment of human neoplasms

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“All evidences about the benefit of physical activity in neoplastic patients support the use of specific training protocols to gain and improve patients' quality of life both during and after cancer treatments.”

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Currently, cancer represents the main leading cause of death in high-income countries, and the second leading cause in those with low and middle income. In 2018, an estimated 1,735,350 new cases of cancer will be diagnosed in the USA with 609,640 dead. The most common cancers detected in the last years are of epithelial origin such as the cancers of breast, lung, prostate, colon and rectum, melanoma of the skin, bladder, kidney and renal pelvis, endometrium, pancreas, thyroid and liver [1].

Despite the recent notable improvement in cancer diagnosis and treatment, primary prevention represents the better approach to significantly reduce cancer-related deaths. Primary prevention is defined as a set of interventions that keeps a cancerous process from ever developing and includes health counseling, education and environmental controls [2]. Thus, we could provide a viable way to decrease the incidence of tumors by identifying the appropriate lifestyle and the environmental risk factors associated with cancer development, educating the public about these risk factors and promoting interventions to modify them.

Lifestyle changes related to the main risk factors such as weight control, regular physical activity, balanced and controlled diet and stress reduction seem to be the milestones for cancer prevention [3]. In fact, there are numerous studies that investigated these aspects to provide ever more complete and clear guidelines for the population. Expert groups of the American Cancer Society and the American Institute for Cancer Research, recommend avoiding smoking, limiting alcohol abuse, minimizing sedentary lifestyle (including television), maintain a healthy bodyweight and eat fruit and vegetables, because these aspects greatly influence the wellbeing of the person and can decrease the risk of developing tumors. The World Cancer Research has estimated that about 20% of all cancer diagnoses in the USA are related to obesity, inactivity, excessive consumption of alcohol and therefore it can be prevented. More in general, of the 7 million cancer-related deaths recorded worldwide every year, 35% were attributable to modifiable risk factors [4].

In a large prospective cohort study based on 900,000 subjects, it was found that elevated values of body mass index (BMI) are associated with an increase in deaths for all types of cancer both in men and in women. In particular, men and women who have a BMI of more than 40 have a 52% and a 62% higher cancer mortality rate if compared with men and women with a BMI <25 [5].

In this scenario, plenty of scientific and solid evidence highlighted the essential contribution of physical exercise in cancer prevention and treatment. Nevertheless, the molecular mechanisms involved in the association between physical exercise and risk of cancer are not clear yet. Therefore, the identification of the molecular determinants

of this association could be essential to promote specific recommendations for the management of cancer patients. The most studied molecules and/or pathways that are involved in both physical activity and cancer homeostasis are sex hormones, metabolic hormones, adipose and inflammation cytokines, immune function, oxidative stress, DNA repair and xenobiotic enzyme systems [6]. Specifically, physical activity seems to lower the levels of circulating sex hormones, thus reducing the incidence of hormonal-related tumors as the cancers of breast, endometrium, ovaries, prostate and testes [6]. In breast, prolonged exposure to estrogens in women induce the neoplastic transformation of epithelium both before and after menopause [7]. In our recent investigations, we reported a putative association between estrogen receptor positive breast cancer cells and the development of bone metastasis from breast cancer [8,9]. However, it is demonstrated that physical activity reduces the incidence of hormone-mediated tumors, not only by decreasing the endogenous production of estrogens and androgens, but also increasing the circulation of sex hormone-binding globulins that capture these hormones inhibiting their ability to stimulate tissues target [10]. Other metabolic hormones and growth factors are influenced by physical activity. For example, regular exercise lowers insulin levels, which is associated with a decreased risk of developing cancer [11]. Another risk factor for cancer development is the chronic inflammation. In detail, a condition of prolonged inflammation in the tissues can dysregulate the cell cycle of normal cells and, at the same time, promote the growth of damaged cells increasing the risk of mass tumor formation. The main biomarkers associated with both chronic inflammatory and cancer are IL-6, C-reactive protein and TNF- α [12]. Studies reported a significant serum decrease of all these serum markers in the early phases of moderate training. Simultaneously, constant physical exercise can reduce both tissutal and systemic inflammation by improving body composition and reducing the rate of inflamed adipose tissue [13,14].

The presence of numerous epidemiological and clinical studies on the benefits of exercise lay the foundation to define guidelines for people affected by neoplastic diseases [15,16]. Although these guidelines have already been disseminated by governmental and nongovernmental organizations, most of the cancer patients do not follow these recommendations. Recent data showed that 60–70% of people with cancer do not adhere to the aerobic exercise guidelines, and 80–90% do not adhere to indications for the resistance exercise [17].

A recent study points out the efficacy of physical exercise in decreasing side effects, before, during and after cancer treatments, and its role in a decreased risk of developing new tumors and comorbidities such as cardiovascular disease, diabetes and osteoporosis [18]. Indeed, being physically active promotes a protective effect against the recurrence of tumors, against specific mortality from cancer and all deaths related to secondary causes of the tumor [18].

The subjects undergoing randomized trials, in which physical activity was prescribed as an adjunctive therapeutic intervention, displayed a significant decrease in adverse effects linked to the administration of anticancer therapy. Epidemiological studies also reported that patients who have practiced physical activity after diagnosis of cancer have a reduced risk of death from cancer, and/or relapse [19,20].

Exercises should be tailored to the characteristics of each patient, considering that specific activity programs for cancer patients must take into consideration their discomfort and adverse effects of the treatments, trying to anticipate the progress of their disorders and their state of health.

All evidences about the benefit of physical activity in neoplastic patients support the use of specific training protocols to gain and improve patients' quality of life both during and after cancer treatments. Exercise guidelines can lead to great physical and psychosocial improvements in cancer patients. These guidelines, recently displayed in *The Lancet Oncology*, recommending 150 min of exercise at moderate intensity, 75 min of high intensity exercise and two to three sessions of training with overloads per week, are apparently consistent with the guidelines for the general population [21].

In line with this, the Public Health Organization recommends 30 min of moderate-to-vigorous physical activity for at least 5 days a week or more. These guidelines do not have harmful consequences so they can be adopted by everyone and not only by those most predisposed to the development of cancer. Therefore, an effective exercise program for cancer patients could include the following three components: an aerobic workout that pumps up your heart rate (outdoors or on a treadmill), jogging, swimming or bicycling; strength training to tone and build muscles (be sure to get instruction if you are new to this type of exercise; light weights are sufficient to maintain strength); and stretching to keep muscles and joints limber.

Scientific dissertation reported here showed the essential contribution of physical activity in the clinical pathways of cancer patients. Thus, the experts in physical education and sports could take part in all meeting of the modern oncological units.

In conclusion, we must remember that often our most recent discoveries ‘come’ from the past; citing Platone “Lack of activity destroys the good condition of every human being, while movement and methodical physical exercise save it and preserve it.”

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