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Physical activity in oncologic patients

Activitatea fizică la pacienții oncologici

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Abstract

General health benefits from regular exercise programs. Among the beneficial effects, improvements in cardiovascular and respiratory parameters, digestive status, muscular and osteoarticular mass and metabolism, neurological and psychic symptoms; endocrine effects and control of body composition and weight; modifications of the immune system and induction of systemic anti-inflammatory effects can be demonstrated. Also, in oncologic patients, exercise programs reduce toxicities and side effects of treatment and improve physiological parameters, physical function, psychological well-being, treatment outcomes and overall health-related quality of life; can reduce even the risks for some cancers.

Implementing regular exercise programs in cancer patients and survivors faces several challenges regarding patient selection and information, psychological factors, design of exercise programs, establishing outcomes, health professionals' perception and even environmental factors. More research is required before exercise gains widespread acceptance.

Key words: exercise programs, beneficial effects, cancer risk.

Rezumat

Sănătatea în general beneficiază de programele regulate de exerciții fizice. Printre efectele benefice, s-au evidențiat îmbunătățirea parametrilor cardiovasculari și respiratorii, a funcției digestive, a masei musculare și osteoarticulare și a metabolismului, a simptomelor neurologice și psihice; de asemenea, s-au demostrat efecte endocrine și controlul compoziției corporale și a greutății, modificări ale sistemului imunitar și efecte anti-inflamatorii sistemice. La pacienții oncologici, programele de exerciții fizice au numeroase efecte benefice: reduc reacțiile toxice și efectele secundare ale tratamentului și îmbunătățesc parametrii fiziologici, funcția fizică, bunăstarea psihologică, rezultatele tratamentului și calitatea generală a vieții; pot reduce chiar și riscurile pentru anumite tipuri de cancer.

Implementarea unor programe regulate de exerciții fizice la pacienții și supraviețuitorii cancerului se confruntă cu mai multe provocări în ceea ce privește selectarea pacienților și informațiile de care aceştia dispun, factorii psihologici, proiectarea programelor de exerciții, stabilirea rezultatelor, percepția profesioniștilor din domeniul sănătății și chiar și factorii de mediu. Este încă necesară o cercetare continuă înainte de acceptarea pe scară largă a beneficiilor induse de programele de exerciții.

Cuvinte cheie: programe de exerciții fizice, efecte benefice, riscul de cancer.

Introduction

A healthy lifestyle can be characterized by: no smoking (never smoking or no smoking for at least 5 years), no or moderate alcohol drinking, a body mass index (weight/height^2) between 18.5 and 27.5, and regular physical activity (vigorous-intensity aerobic exercise for at least 75 minutes or moderate-intensity exercise for 150 minutes) (Song & Giovannucci, 2016). Physical activity means "any body movement produced by the contraction of skeletal muscles that causes substantial energy expenditure beyond resting values" (***, 2014).

Besides diet, alcohol consumption and smoking, the most accessible lifestyle factor that can be modified is physical activity. In all people, including cancer survivors, correcting the status of these factors leads to improvements of health-related quality of life. Especially for physical activity, several studies have found evidence that supports the positive association between health-related quality of life and physical exercise (Gopalakrishna et al, 2016). Also, modification of diet and occupational factors can significantly reduce the cancer burden (Al-Zalabani et al, 2016).

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Health benefits of regular physical exercise

General health benefits from exercise programs such as aerobic, resistance, flexibility, and balance training. Aerobic training, including walking, jogging, cycling, running or swimming, involves large muscle groups, which act in a dynamic and rhythmic manner, for sustained periods of time (Garber et al., 2011).

Exercise as a regular physical activity is the only one that can be efficient against a large spectrum of chronic diseases. The continuous increase of the elderly population also increases the prevalence of the main chronic diseases, including cancer (and also metabolic diseases such as obesity and type 2 diabetes, arterial diseases - hypertension and atherosclerosis, chronic pulmonary, neurodegenerative, kidney and immune-mediated diseases) (Di Raimondo et al., 2016).

The wide range of immediate and long-term health benefits of regular physical exercise is well known, both for young and older adults. Through regular exercise, a lot of physiological, biochemical and even transcriptional changes occur, which improve both mental and physical health (Lindholm et al., 2016). The adaptation of the human body induced by exercise engages signaling mechanisms, specific DNA replication and finally generates new proteins (Coffey & Hawley, 2007). Individual people vary in their responses and the physiological effects of exercise-induced adaptations are determined by the frequency and intensity of physical activity.

The myriad beneficial effects of a regular exercise program include the following:

- cardiovascular parameters improvements - reduced incidence of several diseases such as coronary arterial disease, stroke, hypertension; - through improvements in cardiac power and heart contractility, heart rate variability parameters returned to their baseline values (Hsu et al., 2016); and also, through reductions of blood pressure and reactive hyperemia (Santos et al., 2016), improvement of endothelial function (nitric oxide availability) (Antunes et al., 2016);

- respiratory parameters - exercise training was proved to prevent and contribute to rehabilitation of chronic diseases (Vainshelboim, 2016) through improvements in peak VO_2 values, breathing pattern, dyspnea;

- digestive effects - the gut microbiota strongly interacts with the immune system, can influence health and disease, and it can be modified by physical exercise (Cerdá et al., 2016). This great immunological responsibility of gut microbiota offers therefore to exercise a beneficial role in preventing and ameliorating gut inflammatory diseases (for example, ulcerative colitis) (Cook et al., 2016);

- muscular and osteoarticular characteristics - improvement of bone density, flexibility, muscular strength and endurance, and reduction of risk for falls and injury; the effects of exercise are translated into molecular pathways of all bone cells which will remodel the bone (Castrogiovanni et al., 2016);

- neurological and mental benefits - regular exercise optimizes the sympathetic nervous system as the stress responsive system, reduces emotional and physiological reactivity, and enhances neuroplasticity and growth factor expression (Silverman & Deuster, 2014); also, it increases positive mood and well-being, therefore inducing benefits for cognition and social functioning; it also reduces depression and anxiety (Salmon, 2001);

- endocrine effects - exercise activates the hypothalamic-pituitary-adrenal axis, releases vasopressin (for saving water) and growth hormone (which induces activity of the growth hormone-insulin-like growth factor-1 axis and increases the effects of sex steroid hormones on the structure and function of skeletal muscles) (Jansen, 2016). Exercise also stimulates the release of thyroxin and testosterone, reduces blood insulin concentrations and increases insulin sensitivity, releases epinephrine (which also enhances the ability to use muscles), releases endorphins (which diminish pain sensitivity and can reduce tension or anxiety by inducing a sense of euphoria). Also, exercise improves thymus function, with immunological and fatigue-delaying effects (Kraemer & Rogol, 2005);

- control of body composition and weight - properly selected regular exercise improves total daily energy expenditure (Leońska-Duniec et al., 2016). Adequate aerobic exercise in particular was proved to exert metabolic benefits (Keating et al., 2016);

- the immune system - it works together with the nervous and endocrine systems and it shares the same ability to adapt to physical exercise (especially B lymphocytes) (Fragala et al., 2011). A single intense exercise session (peak aerobic exercise), more than submaximal exercise, more rapidly induces a higher increase of neutrophils, monocytes and lymphocytes (Szlezak et al., 2016) and a decrease in the CD4+/CD8+ ratio (Natale et al., 2003). Regular exercise at a moderate intensity can reduce the incidence of infections (Gleeson, 2007);

- induction of systemic anti-inflammatory effects - longer duration exercise is more efficient in creating an anti-inflammatory state - through increases in interleukins 10 and 6 (Cullen et al., 2016). Also, regular exercise reduces the mass of visceral fat and subsequently decreases the release of adipokines (Gleeson et al., 2011), diminishes TNF-α and upregulates the mitochondrial antioxidant system (Antunes et al., 2016). Therefore, regular exercise has steady anti-inflammatory effects that can protect against chronic diseases, which are regularly associated with systemic inflammation.

Effects of regular exercise in oncologic patients

The lack of regular physical exercise and a sedentary lifestyle increase mortality by all causes, including cancer. For example, a study involving physically inactive middle-aged women (less than 1 hour of exercise per week) showed a 52% increased mortality by all causes, a doubled cardiovascular mortality and a 29% increase in cancer-related mortality, compared with physically active women (Hu et al., 2004).

The majority of cancer survivors have low levels of physical activity and do not participate in recommended exercise programs, which increases the disease risks and health care costs (Irwin, 2009). The factors that can limit the participation of oncologic patients in physical activity programs and therefore diminish cancer outcomes are correlated, in addition to toxicity to therapy, with:

comorbidities, a poor baseline health status, functional limitations, cognitive decline, and limited social support (Mohile et al., 2012). Besides, in older adults, cancer diagnosis and its treatments accelerate the physical and emotional decline (Kilari et al., 2016).

Among cancer survivors, the most frequent are obesity and a sedentary lifestyle. An increased number of studies have shown that low levels of physical activity and obesity are statistically significantly associated with cancer recurrence and death (Irwin, 2009). Also, obesity and type 2 diabetes mellitus are common and significant conditions among adult survivors of childhood cancer (Barnea et al., 2015).

Exercise activities designed to optimize balance, flexibility, and strength have multiple positive effects on numerous domains that can be used as indicators in order to assess the positive outcomes: physiological parameters - improvements including immune function, cardiovascular endurance, strength, balance, body composition, lean mass and bone mass (Fairman et al., 2016; Irwin et al., 2009); physical function - through performance indicators, self-reported functioning and symptoms; psychological well-being - it can ameliorate fatigue, insomnia, anxiety, cognitive decline, and increase independence and overall health-related quality of life (Brown et al., 2011; Irwin et al., 2009; Tang et al., 2010; Kilari et al., 2016). In addition to all those mentioned above, regular physical activity was shown to reduce toxicities and side effects of treatment and to exert positive effects on treatment outcomes (Kilari et al., 2016).

Most studies (randomized control trials) have proved the beneficial effects of routine physical activity in breast and prostate cancers. The improvements shown were the following: increase in functional status and physical activity and significant increase of the diet quality index (in breast and prostate cancer) (Demark-Wahnefried et al., 2006); significant increase in physical function (measured on the Short Form-36 subscale), physical activity, quality of life, and significant decrease of the body mass index (in breast, prostate and colorectal cancer) (Morey et al., 2009); preservation of lean mass, diminution of fatigue and psychological distress, increase of lower body function and significant increase of muscular strength and social functioning (in prostate cancer) (Cormie et al., 2015); reduction of disability, increase of objective and self-reported physical function, and significant increase of bench press and leg strength (in prostate cancer) (Winters-Stone et al., 2015); decrease of cancer related fatigue and global side effect burden (in breast and other cancers) (Sprod et al., 2015).

However, a stronger prescription of physical activity in order to be routinely implemented in all cancer subtypes is still necessary; therefore, more studies are required to convince patients and clinicians about the positive effects of a routine exercise and to gain widespread acceptance. Exercise should be adapted to the needs of cancer survivors and focused on the need to improve the targeted outcome. Research for an adaptive exercise program must focus on current knowledge gaps and investigate more accurately whether tumor, clinical, or risk factor characteristics are significantly associated with the effects of physical activity. An adequate study, with cancer-specific biomarkers and disease endpoints, such as recurrence, can convince and can lead to integration of exercise regimens into anticancer therapy (Kilari et al., 2016).

Regular exercise in cancer prevention

In chronic disease of the non-cancer population, regular exercise has shown well-proven benefits in both primary and secondary prevention. However, there are also epidemiological studies showing that increased physical activity via regular exercise reduces the overall risk of cancer recurrence and cancer mortality; significant associations were mainly evidenced for breast and colon cancer specific mortality (Ballard-Barbash et al., 2012; Betof et al., 2013). Also, some studies demonstrated that regular physical activity fights the negative effects of sedentary jobs and can reduce the risks of prostate cancer (Noonan & Farrell, 2016) or bladder cancer (Song & Giovannucci, 2016).

The prevention of post-surgery complications requires exercise-based rehabilitation techniques. Complications such as upper limb lymphedema, mobility impairment and reduced muscle strength and function, defective posture alignment, fatigue and low physical endurance, lung complications, psychosocial difficulties, all require rehabilitation techniques (Irsay et al., 2014). For example, a routine exercise program is very important in recovery after breast surgery and in preventing or treating lymphedema (Puşcaş & Tache, 2015). Similarly to other therapy options (surgery, chemotherapy, radiotherapy, hormone therapy, targeted therapy, etc.), medical rehabilitation plays an important role in establishing the patient's body function and quality of life (Irsay et al., 2014).

Designing exercise programs for cancer patients

Regular exercise programs have shown efficacy in ameliorating both the physical and psychological impairments induced by cancer and its treatment. Rehabilitation programs reduce fatigue, pain or dyspnea, increase physical functionality and improve the quality of life. Major benefits of kinesiotherapy have been demonstrated by several recent studies; this is an argument for the need to initiate rehabilitation exercise programs as soon after surgery as possible (Irsay et al., 2014).

The implementation of a regular program and the recruitment of cancer patients in clinical trials that are able to prove the efficacy of those programs encounter several barriers at different levels:

- patient selection and information - patients with low baseline functional status are excluded; breast and prostate cancer survivors are predominantly recruited; the chosen population is racially and ethnically homogeneous; some programs only accept patients who have completed all forms of treatment; selection is not based on individual physical activity needs; the individual risk level of exercise and contraindications for the exact type of physical activity are not assessed; limited information of patients regarding the active treatment of cancer and about where they should go to obtain this information from a professional; limited adherence of patients to clinical studies (Kilari et al., 2016);
- psychological factors - interest in exercise, beliefs

about the importance of exercise and lack of information about the potential benefit of exercise interventions and the available resources for exercise programs;

- design of the exercise program – it is not adapted to the type and stage of cancer or treatment; it is not integrated into cancer care; it tends to be short (usually 4–12 weeks); exercise sessions are in a group format and are not personalized to patient status, needs or patient lifestyle (in terms of frequency, duration, intensity or mode); it does not provide feedback after the completion of the study; adverse events are often not considered or known; quality of life concerns are not routinely addressed throughout the course of the exercise program (Kilari et al., 2016);

- establishing outcomes - the impact of the exercise intervention on cancer outcomes is not regularly assessed; the outcomes centered on the patient are not prioritized; some functional outcomes are not routinely measured; the long-term effects of exercise programs on outcomes are unknown (Kilari et al., 2016);

- health professionals' perception - clinician fears of toxicity, limited information about the role of exercise in improving physical status and activity; an exercise physiologist or a physiotherapist can sustain physical activity participation through research evidence;

- environmental factors - occupational status, lack of time and bad weather (Chou et al., 2016).

Some measures that can help to overcome the above mentioned barriers could be:

- for patient selection - education about the role of exercise in improving physical fitness and cancer prognosis; involvement of the patient and community from the beginning; the programs should be designed and tested along the whole cancer continuum (diagnosis, active treatment, post-treatment);

- for the design of the exercise program - must be based on individual physical activity needs (cancer type, therapy, physical limitations and comorbidities); must be adapted to the targeted outcome; needs to provide feedback and to be increased gradually, based on participant tolerance; needs to be designed with the community in mind (e.g., considering transportation, parking, time of day, etc.);

- for health professionals' involvement - all health professionals must ally and integrate into clinical trials (particularly physiotherapists or exercise physiologists);

- for establishing outcomes - needs a better understanding of the complexity of older patients with cancer; needs to be relevant to patients (functional and quality of life outcomes are more relevant than maximal aerobic capacity); in order to ensure relevance and feasibility of outcomes of interest, feedback and involvement from all health professionals are required.

Regarding the duration and type of exercises, the American College of Sports Medicine (ACSM) published public health recommendations for exercise among cancer patients and survivors. A supervised and personalized program (a combination of muscular strength/endurance and cardiovascular endurance exercises) is safe, has no risks and has a greater potential of improving physical functions than a general program (Anderson et al., 2012). An exercise program significantly influencing ACSM recommends that "patients and survivors exercise at least 150 minutes per week of aerobic activity on most days of the week at a moderate intensity level or 30 minutes of vigorous aerobic activity 3 days of the week, accompanied by at least 20-30 minutes of resistance activity 2 or more days per week" (1; Rock et al., 2012; Chou et al., 2016). It is recommended to cancer patients and survivors to start low, progress slowly and get help from qualified professionals. Despite these published public health guidelines, it is estimated that up to 70% of cancer survivors do not meet these ACSM public health recommendations (Irwin, 2009). The two main reasons for this are 1) a lack of awareness among health care providers, patients, and survivors of these exercise recommendations, and 2) a lack of understanding about how to provide precise exercise prescriptions for individuals to effectively treat specific cancer and treatment-related outcomes.

An example of exercise program at a community center could be (Desveaux et al., 2016): 1) warming up (10 minutes, with gentle stretches for all major muscle groups - neck, shoulders, arms, hamstrings, quadriceps, and calves; marching on the spot to increase heart rate); 2) aerobic training (20-30 minutes, walking along a designated track with rests as needed, cycling and/or treadmill); 3) functional exercises to promote strength and balance (20-30 minutes - free weights and 'wall climbing' for upper extremity; mini-squats, stairs, hip abduction and hip extension while holding onto the back of a chair with bands available to add resistance for lower extremity; basic balance exercises such as practicing tandem stance, standing on one leg, walking on different surfaces (with mats and rails available for safety); 4) cool down (10 minutes, with gentle stretches for all major muscle groups - neck, shoulders, arms, hams, quads, and calves; slow walking to decrease heart rate). Each exercise targets specific muscle groups and exercises are commonly performed using groups of 2-4 sets (Chodzko-Zajko et al., 2009; 1). For conferring confidence to patients, the program's proximity and health care professional support should always be kept in mind.

Researchers have also utilized aqua aerobics with cancer survivors (in breast cancer); this reduces axial loading and allows participants to perform exercises they may not be able to do on land (Cantarero-Villanueva et al., 2013; Fernandez-Lao et al., 2013).

The final aims of all those measures are to decrease hospitalization, reduce cancer treatment toxicity, increase the disease-free period and overall survival and even contribute to cancer prevention.

Overall, promoting an active life improves quality of life and in order to achieve this goal, all segments of society should collaborate with one another.

Conclusions

1. Commonly, after development of a cancer, physical activity is reduced.

2. A greater physical activity level decreases the risks of cancer and increases the quality of life, before and after surgery.

3. Regular physical activity as a lifestyle modification can represent a primary prevention measure for cancer control, and alleviates the important burden of cancer for the health system.

4. Implementing exercise programs for cancer patients and survivors requires measures regarding patient education, program adaptation based on individual activity needs, establishing relevant outcomes, health professionals' involvement.

5. Further research is required before exercise gains widespread acceptance.

Conflicts of interest

There are no conflicts of interests.

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