Review

Limitations on Physical Activity in Childhood Cancer Survivors and Intervention Programs: A Review of Literature

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ABSTRACT

Purpose: Pediatric cancer survivors have been increased through the last decades, while scientists conduct studies in order to discover new treatments and ameliorate survivors' quality of life. Physical activity consists an important factor with multiple benefits for the overall health of Childhood Cancer Survivors (CCSs). However, CCSs are not following the suggested guidelines and they are defined by low physical performance. The aim of this review was to highlight the reasons survivors neglect exercise and how intervention programs benefit them.

Methods: Search was conducted for studies published between 2002 to 2021 in four databases (PubMed, Goggle Scholar, Cochrane Library and Research Gate). All studies were in English language. All articles were either descriptive or intervention research and provided results according to survivors' physical activity and specifically related to the barriers, preferences and benefits.

Results: Results showed that survivors face mostly physical and psychological barriers that discourage them from exercise. Intervention programs showed significant improvement in several aspects of CCSs' physical and mental health and social life. While some survivors are not particularly active, they reported willingness to improve not only the level of physical performance but also several unhealthy habits.

Conclusion: Appropriate guidance and specialized framing by professionals are crucial not only for CCSs but also their families. Further research is necessary in order to reassess and ameliorate beneficial policies and promote Public Health for CCSs.

Key Words: *Childhood Cancer Survivors (CCSs), Psychosocial Barriers, Physiological Barriers, Public Health, Physical Activity*

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Introduction

In 2020, the worldwide incidents of childhood cancer were 206,362 between the ages of 0 and14 years. The most common diagnoses at these ages were leukemia, brain and central nervous system (CNS), non – Hodgkin lymphoma, kidney cancer and Hodgkin lymphoma (1). According to the World Health Organization, cancer is a leading cause of mortality in children and adolescents (2). Specifically, the American Cancer Society reports cancer as the second cause of death in this population, after accidents (3).

Regardless the type of cancer, 80,104 cases of death were reported in 2020 internationally. Particularly, 25,080 (31.3%) cases were due to leukemia and 11,889 (14.8%) due to CNS tumors. Although it is estimated that by 2025 the percentage of mortality in Africa will be increased by 9.2%, a decrease of 1.3%, 2.2% and 2.7% in mortality is expected in America, Europe and South-East Asia respectively (1).

The scientific community has developed different types of childhood cancer treatment. Most common treatments are chemotherapy, radiation therapy, surgery, immunotherapy and stem cell transplant, separately or in combination. The eligibility of a treatment depends on the type and the stage of cancer (4). Despite the received treatment, some people may develop second cancers either as a long-term effect of the initial malignancy or due to the treatment. The second cancer as a new and completely different cancer may not be associated with the first one and its completely different from the cancer recurrence which means that the original cancer reoccurs (5).

According to National Cancer Institute someone who has been diagnosed with cancer, is known as survivor from that moment until the end of life (6). In order to improve the general health and quality of life (QoL) of cancer survivors, several guidelines are recommended. The most important among them is to be active and to participate in physical activity gradually (3).

Objective of the present review is to investigate the level of physical activity in childhood cancer survivors (CCSs) and its contributing factors. Furthermore, the intervention programs aimed to improve and motivate CCSs to be physically active were reviewed.

Methods

A literature search was conducted for studies published any time since 2002, in four databases: PubMed, Google Scholar, Cochrane Library and Research Gate. The studies in this review had to meet three inclusion criteria: 1) reference in CCSs of any age, 2) any type of cancer, 3) written in English language. No restrictions were considered regarding geographical origin or whether survivors were on/off therapy.

Results

Study Designs and Samples

In this review two meta – analyses (7,8), two systematic reviews (9,10), one systematic review and meta – analysis (11), six randomized controlled trials (12–17), one pilot clinical trial (18), one quasi – experimental study (19), five cohort studies (20–24), seven case–control studies (25–31), eight cross–sectional studies (32–39), one cross–sectional cohort study (40) and four qualitative studies (41–44) were included.

Out of the 38 studies, 15 were conducted in the USA, 11 in Europe (Sweden, Spain, Italy, France, Germany, UK, The Netherlands, Greece), six in Asia (China, Turkey), three in Canada and three in Australia. Four studies were based on data from participants in the Childhood Cancer Survivor Study (CCSS) (22,24,30,35), two based on data from Swiss Childhood Cancer Survivor Study (SCCSS) (29,33)and two from St. Jude's Lifetime Cohort Study (14,20).

According to sex, the majority of participants were male. The most common diagnoses were hematological malignancies and CNS tumors. The types of treatment were chemotherapy, radiation therapy, surgery, bone/cell marrow transplant or mixed methods.

Data from the final 38 studies are presented in Table 1, including: authors/year and country, study design, sample characteristics, type of cancer and outcome measures.

Level of physical activity in CCS

Several studies included in the present review demonstrated a reduced physical activity of CCSs (8,10,24,25,27,31). Especially malnourished survivors had a significantly lower physical performance than well-nourished CCSs (P=0.01) (27). As Gülnerman et al. reported, even after a long time since completion of therapy, the physical capacity of CCSs was significantly lower as compared to their healthy siblings (25). Furthermore, Ness et al. showed that survivors, when compared with their healthy siblings, were almost twice more likely to have performance limitations (RR, 1.8; 95% CI, 1.7-2.0) (24). Apart from limitations in physical activity and performance, survivors were 4.7 times more vulnerable to restrictions in personal care and daily activities (RR, 4.7; 95% CI, 3.6-6.2) (24).

The level of physical activity was associated with CCSs age and sex (17,22,28,29,39). One study revealed the physical inactivity, among other factors, as a behavioral risk factor (17). Older CCSs had higher behavioral risk factor index scores. Furthermore, one study showed that limitations in sports were more frequent in CCSs aged ≥40 years (OR 2.7, 95% CI, 1.02-7.16) (29). In the study of Paxton et al. differences were identified between adolescents and adults CCSs (39). Specifically, leisure time physical activity (LTPA) was significantly correlated only to improved physical function in adult CCSs (P<0.01), whereas in adolescent CCSs, LTPA was associated with improved overall health related QoL, social and cognitive function and cancer worry (all P<0.01). Another study, examined the relationship between sex and level of exercise capacity as measured by the related VO2max (ml/kg/min) (28). Vo2max refers to the maximum volume of oxygen that the body can use during exercise. The survey showed that female survivors had lower mean VO2max than their healthy siblings (P=0.03) (28).

Frequency, intensity and duration of exercise had a significant impact on the level of physical activity in CCSs. Lanfranconi et al. showed that exercise over time is very important, even if the intensity is low to moderate, such as a 6-min of walking (21). Similar results were demonstrated in the work by Scott et al.,where a 6-MET-h/wk (metabolic equivalent tasks) increase in vigorous exercise was associated with a 13% reduction in the rate of death from any cause (22). The same researchers highlighted the benefits of continuous exercise, while increased exercise over 8 years was related to an adjusted 40% reduction in the rate of death from any cause (RR, 0.6; 95% CI, 0.44-0.82) (22). Other two studies revealed the importance of frequency, intensity and duration of physical activity in cognitive, psychological and physical function of CCSs (35,38). Badr et al. observed that CCSs who had better physical function scores exercised more often (P=0.01), while those who expressed more general fatigue (P=0.04) and cognitive fatigue (P=0.01) exercised less often (38). Additionally, Tonorezos et al. found association between vigorous exercise and a lower prevalence of depression (Ptrend=0.003) and somatization (Ptrend=0.005) (35).

Limitations on physical activity

Despite the aforementioned studies, other studies focused on the reasons why CCSs report low physical activity levels (17,20,23,24,26,29,30,32–34,36,37,41,42,44). All of them referred to physiological limitations.

Specifically, a self-reported survey highlighted that among 20 participants, 11 did not exercise and 3 invocated current health conditions (42). Another study showed that severe headaches discouraged CCSs from working out (44). Four studies correlated limited physical performance with the occurrence of neurological and musculoskeletal impairments (24,29,33,44). Moreover, in the survey of Ness et al., CCSs with musculoskeletal impairments (RR, 1.9; 95% CI, 1.7-2.0) and CCSs with neurologic impairments (RR, 2.0; 95% CI, 1.9-2.2) had the highest risk for developing a performance limitation as compared to CCSs without similar comorbidities (24). Five self-reported studies demonstrated the crucial impact of pain, fatigue and decreased physical strength on physical activity status (29,32,34,36,44). However, in the work by Nayiager et al. CCSs who had a fracture during the treatment for acute lymphoblastic leukemia reported more active hours (mean 8.8 vs. 6.9, F=6.14, P<0.01) on a typical weekend day (40).

One study examined the impact of cardiac impairments in physical activity of CCSs; especially those who had cardiac problems had a twice as high risk to present performance limitations, when compared with their healthy siblings (RR, 2.0; 95% CI, 1.8-2.2) (24). Another study investigated the exercise tolerance by measuring peak oxygen uptake and reported that tolerance was significantly better among survivors without cardiac autonomic dysfunction (CAD) (24.4±8.1 vs. 21.2±10.1 mL/kg/min, P<0.001) as compared to survivors with CAD (20).

Regarding the percentage of oxygen volume (VO2peak), two studies associated it with physical activity level (20,26). Papalia et al., found that VO2peak was significantly higher in the control group than in brain tumor CCSs (43.3±11.9 and 32.4±10.2 mL/kg/min, respectively, P=0.04) (26). Furthermore, survivors had decreased exercise tolerance, as measured by peak oxygen uptake (24.2±6.1 vs. 27.7±8.0 mL/kg/min, P<0.001) when compared with controls (20).

Another study found statistically significant differences between participant z scores and the normative sample on balance (P<0.001; 95% CI, -1.66 to -0.97) and running speed/agility (P=0.005; 95% CI, -1.04 to -0.20) (37).

Despite the physiological barriers, physical inactivity was detected in CCSs due to psychological problems (29). Moreover, depressive symptoms, coexisting with conflicts with the parents, constituted a risk factor for physical inactivity (β=0.005, P<0.05) (17). Krull et al., reported correlations between social withdrawal (OR 1.7, 95% CI, 1.2-2.5, P=0.01) and use of anti-depressants (OR 3.2, 95% CI, 1.1-1.7, P=0.02) with physical inactivity in adulthood (30).

Furthermore, some studies included in this review referred to the type of diagnosed cancer and the type of received treatment as factors that affect the exercising status of CCSs. Rueegg et al., showed that CCSs are more likely to report restrictions in sports if they had been diagnosed with a CNS tumor (OR 7.1; 95% CI, 3.7-13.8), a retinoblastoma (OR 5.6; 95% CI, 1.7-18.7), a bone tumor (OR 12.3; 95% CI, 5.4-28.2) and a soft tissue sarcoma (OR 3.5; 95% CI, 1.4-8.9) (29). Similar research findings arose from the study by Ness et al., CCSs of bone cancer were 2.9 times (95% CI, 2.6-3.3 times), CCSs of brain cancer 2.5 times (95% CI, 2.2-2.8 times) and CCSs of Hodgkin lymphoma 1.8 times (95% CI, 1.6-2.0 times) more likely to report a physical performance limitation as compared to their healthy siblings (24). One study showed that children with a cancer relapse had lower levels of physical activity (OR 0.5; 95% CI 0.4-1.0, P=0.030) (33).

According to the type of the received treatment, CCSs who received radiotherapy or chemotherapy reported decreased physical performance (24,29,37,42). Specifically, limitations in physical activity were more frequent in CCSs who received radiation, than in CCSs who underwent only surgery (RR, 1.4; 95% CI, 1.1-1.7) (24). However, Nayiager et al., found no statistically significant difference in physical activity between children who received cranial irradiation and those who did not (40).

Additional factors that contribute in physical inactivity of CCSs are associated with daily routine. Some CCSs reported complains about the screening time, the lack of time and scheduling conflicts (23,32,42). The lack of time was also highlighted as a burden by the parents of CCSs in the study by Cheung et al. (41).They reported that family responsibilities limited the time that could be expended in physical activity with their children (41). About half of the children and adolescents cancer survivors expressed that they had limited time for physical activity due to demanding academic responsibilities (36,41). Similar results were found in the survey by Cheung et al., where more than the half of the parents stated that their children were spending a lot of time on homework and had limited time for physical exercise (41). According to Mizrahi et al., another limiting factor could be the insufficient guidelines for the type, intensity and duration of the exercise (32). Furthermore, in the study by Bertorello et al., participants reported that they were physical inactive due to laziness (19%) or because they were not interested in exercising (27%) (23).

Enablers of CCSs and preferences in physical activity

In the present review, two studies concerning the enablers which CCSs found that could motivate them to participate in physical activity, were included (32,42). CCSs noted the importance of physical activity in health and its improvement, as well as in the strengthening of muscles (32,42). In addition to the benefits in physical health, a positive effect in their mental health was reported, even if some participants found physical activity just satisfying and (32,42). CCSs also mentioned that motivation from family or friends was important (32,42).

The preferences for physical activity, as mentioned by CCSs, were demonstrated in three self-reported studies (23,38,42). The cost of the exercise was crucial, while the choice between individual or group training was not important (42). In the same survey, the majority of CCSs showed preference for afternoon or evening training, three days per week, 60 min at each exercise session, on a private gym (42). They also stated that they preferred combining both aerobic and resistance training (42). Furthermore, in the study by Bertorello et al., male participants reported as the most frequent physical activities, soccer and swimming (23). Respectively, the most frequent activities among females were dancing and swimming (23). CCSs also reported that they prefer competitive sports (23). Finally, as shown by Badr et al. , 87% of the participants were disposed to “get in shape”, 84% to be informed about a nutritious diet plan and 75% were “very” or “extremely” interested in joining weight control programs (38).

Physical activity intervention programs

The intervention programs included in the present review aimed to give prominence to the impact of physical activity in general, mental health and QoL. The term QoL refers to cardiorespiratory system, muscles and flexibility (11).

A 16-week randomized controlled trial with gradually increasing intensity training showed that in the intervention group there was a significant positive change in the measurement of VO2peak (12). However, 9 out of 19 articles included in meta–analysis of Morales et al., showed no significant difference in VO2peak (P=0.065, 95% CI,0.12–4.06) (7). Three studies detected a significant improvement in physical functioning in CCSs (14,18,19). The first one, included a 10-week pilot program in Cologne, Germany in which the intervention was the indoor wall climbing (18). Improvement was detected in ankle DF-ROM (dorsiflexion – range of motion) and ankle DF strength (18). Secondly, a quasi - experimental study which investigated the impact of Stoplight Program (SLP), a physical therapy intervention, showed that the intervention group had higher scores in motor proficiency and physical activity (19). Thirdly, a randomized controlled trial examined a web – delivered

physical activity intervention (14). Motivation for activity was represented by an avatar, unique for each participant, which gathered points as a reward for physical training (14). Results showed a significant improvement in fitness measures (handgrip strength, number of sit-ups and pushups) (P<0.01) (14).

Physical activity also contributes to the decrease of cancer-related fatigue in CCSs (13,15). According to an adventure - based clinical trial, after a 12–month period follow up, there was a substantial change in cancer-related fatigue (P<0.001) (15). The self-reported questioners in the randomized controlled trial by Lokkart et al., provided similar results in comparisons between CCSs and healthy population (13). Interestingly, there was a significant difference regarding fatigue in children aged between 7-12 years during a 12-month follow-up (13). Apart from the self-reports of CCSs, parents were also asked about cancer-related fatigue in their children (13). A prominent difference in cancer-related fatigue was described for adolescents aged between 13-18 years, after a 12-month follow-up (13).

Some studies report that the physical activity also contributes in mental health and QoL. Däggelmann et al. highlighted the enhancement in emotional functioning; specifically, participants reported that felt stronger and more self-confident (18). Similar data were derived from the clinical trial by Li et al., where CCSs felt greater self-efficacy, improved QoL and physical activity (15). Two studies in the systematic review and meta-analysis of Mizrahi et al. and the randomized controlled trial of Howell et al. showed that distance-delivered intervention programs contribute to the improvement of psychosocial and physical function, and QoL (11,14). However, the level of physical activity were not significantly increased (11,14).

A qualitative study conducted in greek CCSs showed similar results. CCSs were described as happier, stronger and more active (43). An improvement in physical, psychological functioning and easiest socialization was observed (43).

Physical function of CCSs and psychological function of both CCSs and their families may also be enhanced by the participation in summer camps. A systematic review of 19 observational articles highlighted the decrease of sedentary life and the increase of physical activity, self-efficacy, self-confidence and socialization (9). Moreover, this study revealed the view of the parents of CCSs, who reported that felt more accepted by other families as they had similar experiences due to cancer diagnosis and treatment (9). Three studies from this systematic review showed the positive impact of camps in families' reconnection without distractions of everyday life, such as television (9). In two studies, parents reported that camps were a "safe place" where they can escape from daily life (9).

Another pilot study developed a summer camp in the gym of a pediatric hospital in USA for five months during summer (16). The intervention group participated in several physical activities and the control group just received monthly newsletters with suggestions about physical activity. The findings from the monitor that measured the hours of physical activity showed that the intervention group increased the exercising hours (except from 2 participants). On the contrary, the control group decreased the hours of physical activity (except from 1). A medium effect size (r=0.55) between moderate-to-vigorous physical activity and total self-efficacy scores was also detected, as well as a medium effect size (r=0.62) about subscale for adequacy (19).

Discussion

This paper summarizes the literature of limitations that discourage CCSs from exercising, as well as related intervention programs. This field of study is of particular importance for the enhancement of QoL of CCSs. QoL is also important for the public health as it means "the ability to perform everyday activities which reflect physical, psychological, and social well-being" and "patient's satisfaction with levels of functioning and the control of disease and/or treatment – related symptoms" (45).

The present review showed that CCSs have decreased physical performance due to several barriers. However, it is encouraging that several studies indicated the willingness of CCSs to participate in physical activities and to overall improve physical and mental health (23,38,42). In order to accomplish that, framing by qualified health professionals is considered crucial. Specifically, apart from medical experts, collaboration with nutritionists seems to be beneficial, as Alford et al. (27), Rokitka et al. (42) and Badr et al. (38) highlighted. Physiotherapists also, provide services targeting to the improvement of motor and physical mobility (19). Cooperation with mental health professionals could be profitable for the management of psychological and social barriers.

The intervention programs included in this review, showed that physical activity level can be increased and health, especially mental, can be improved. As Kelada et al. mentioned, except from CCSs, families can be also positively influenced (9). Further research on enablers and preferences of CCSs could pave the way to intervention programs that focus on the needs of CCSs and their families.

Limitations should be considered when interpreting the results of this review. Firstly, the sample of some studies was small and only studies in English were included. Secondly, among all studies, eight were cross–sectional and four quantitative and some of them had not statistical data.

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