



Review article

Optimizing diet and nutrition for cancer survivors: A review

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ABSTRACT

The number of cancer survivors is increasing and they are often highly motivated to search for information about nutrition and about physical activity in order to try to improve their treatment outcomes, quality of life and overall survival. In the light of these concerns, the World Cancer Research Fund (WCRF)/American Institute for Cancer Research (AICR) as well as the American Cancer Society recommend a largely plant-based diet with limited consumption of red and processed meat, and limited consumption of alcohol, as well as the maintenance of a healthy weight throughout life and regular engagement in physical activity. There is a need for well-designed large observational and intervention studies to shed more light on the association between diet and cancer survivorship, and to suggest additional means for the secondary prevention of cancer.

1. Introduction

Cancer is the second leading cause of death globally, irrespective of socio-economic context, since it is the second leading cause of death in high-income countries and the third leading cause of death in low- and middle-income countries [1,2]. It was estimated that there were approximately 14 million new cases of cancer in 2012 [1,2]. Cancers such as lung, breast and colorectal are on the rise, in both developed and developing countries, due to the adoption of lifestyles that are known to increase risk of the disease, such as poor diet, smoking and lack of physical activity [1]. According to the World Health Organization (WHO), cancer was responsible for 8.8 million deaths in 2015 [2], and this is expected to grow to 13 million cancer deaths simply due to the growth and aging of the population [1]. At the same time, progress in the early diagnosis and management of the disease has led to increases in both cancer survival rates and survivors' life expectancy. As a result, in less than 10 years from now, it is estimated that the population of cancer survivors will increase to 20.3 million [3].

A cancer survivor is defined as anyone with a history of cancer, from the time of the diagnosis through the remainder of their life. Cancer survival is characterized by three phases: 1) the time of diagnosis to the end of initial treatment and recovery; 2) the transition from treatment to extended survival, including survivors who are disease free or who have stable disease; and 3) long-term survival [3]. Cancer survivors are mostly individuals who have been diagnosed and treated for breast, colorectal and prostate cancer, since these types have usually the best 5-year survival. Moreover, since cancer is a disease associated with aging, nearly half (47%) of survivors are 70 years of age or older, while only

11% are younger than 50 years [3]. Cancer survivors usually face several long-term health and psychosocial consequences of their treatment, including cardiovascular complications, endocrine disorders, osteoporosis, cognitive deficits, dental caries/complications as well as weight changes [4]. These consequences, combined with the morbidity and mortality associated with the disease itself, and its potential for recurrence, make it obvious that there is a growing need for recommendations on lifestyle choices for cancer survivors. It is well demonstrated that lifestyle factors (diet, alcohol, obesity, tobacco use etc.) lie at the root of noncommunicable diseases such as cancer [5,6], cardiovascular diseases [5,7] and even dementia [8].

The aim of this review is to present the current evidence-based guidelines on diet, as well as physical activity, for cancer survivors, in order to identify the gaps in knowledge.

2. Data sources and searches

Data on cancer survivors' lifestyle behaviors, and especially dietary habits and choices, have been accumulating over the past decades. However, few observational studies have reported associations between diet and cancer survival, and those that have done so have been very diverse, leading to a lack of definitive evidence. As a result we did not perform a literature search using electronic databases (i.e., Medline via Pubmed and Scopus) but instead discuss here the current recommendations for cancer survivors produced by all the relevant organizations, i.e., the Second Expert Report: Food, Nutrition, Physical Activity and the Prevention of Cancer: a Global Perspective, published in 2007 by the World Cancer Research Fund/American Institute of Cancer

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Research, as well as the American Cancer Society Guidelines for Nutrition and Physical Activity for Cancer Survivors published in 2012.

3. Nutrition and physical activity for cancer survivors

3.1. Dietary choices

In 2007, the World Cancer Research Fund (WCRF)/American Institute for Cancer Research (AICR) updated its previous extensive systematic review of the evidence linking food, nutrition and related factors to cancer. It also addressed cancer survivors and concluded that due to the lack of sufficient research evidence, they should be encouraged to follow the recommendations for primary cancer prevention [9]. Firstly, in this review, the *Panel* suggests that a cancer survivor should eat mostly foods of plant origin. More specifically, it is proposed that cancer survivor should eat at least five portions/servings (at least 400 g or 14 oz) of a variety of non-starchy vegetables and fruit every day, eat relatively unprocessed cereals (grains) and/or pulses (legumes) with every meal and limit their intake of refined starchy foods [9]. Moreover, the intake of red meat should be limited to less than 500 g (18 oz) a week, while it was noted that very little if any processed meat should be consumed. Furthermore, a cancer survivor should avoid salt-preserved, salted or salty foods. An intake of less than 6 g of salt (2.4 g sodium) a day was recommended, while it was also proposed not to eat mouldy cereals (grains) or pulses (legumes). In addition to the above, energy-dense foods as well as fast foods should be consumed sparingly, and sugary drinks should be avoided [9]. The *Panel* also noted that consumption of alcohol should be limited to no more than two drinks a day for men and one drink per day for women [9].

The Nutrition and Physical Activity Guidelines for Cancer Survivors published in 2012 by the American Cancer Society (ACS) seem to be consistent with the WCRF/AICR recommendations. Indeed, the ACS proposed the consumption of a healthy diet with emphasis on plant foods. More specifically, a cancer survivor was recommended to eat at least 2.5 cups of vegetables and fruit every day, to choose whole grains instead of refined grain products, and to limit their consumption of red and processed meat [10]. Finally, the consumption of alcoholic beverages should be limited to no more than 2 drinks per day for men and 1 drink per day for women [10].

In a recently published systematic review and meta-analysis of cohort studies, in which 117 studies enrolling 209 597 cancer survivors were included, the aim was to investigate the association between food intake and dietary patterns and overall mortality among cancer survivors. Schwedhelm et al., [11] reported a low risk of mortality for cancer survivors with the highest intakes of vegetables and fish, while alcohol consumption was associated with an increased risk of overall mortality. Furthermore, prudent/healthy dietary patterns were associated with a decreased risk of mortality, whereas Western dietary patterns resulted in the opposite outcome for the cancer survivors [11].

These results seem to be in full agreement with the above guidelines. Food groups like fruits, vegetables, fish and whole grains seem to have a protective role against cancer, while alcohol as well as red and processed meat should be avoided, not only in an effort to prevent cancer primary, but also when trying to avoid mortality from the disease or recurrence. The constituents of these food groups seem to explain, at least to some degree, the biochemical mechanisms by which diet can affect tumor pathogenesis. Indeed, fruits and vegetables are sources of a wide variety of micronutrients and other bioactive compounds, including antioxidants like vitamin C and E, folate, dithiolthiones, carotenoids, glucosinolates, indoles, isothiocyanates, protease inhibitors and phytochemicals (lycopene, phenolic compounds, flavonoids etc.), which seem to have anticancer properties [12,13]. Furthermore, all these compounds may act against cancer through their antioxidant, anti-mutagenic and anti-proliferative properties, and also have the ability to stimulate the immune system, trap free radicals and modulate hormone concentration and metabolism [12,13].

A great number of systematic reviews and meta-analyses of prospective studies have concluded that intake of whole grains is associated with a reduced risk of coronary heart disease, cardiovascular disease, all-cause mortality but even more with total cancer as well as breast and colorectal cancers [14–16]. Whole grains are concentrated sources of dietary fiber, which tends to increase fecal bulk and decrease the transit time. Decreased transit time gives less opportunity for fecal mutagens to interact with the intestinal epithelium, and in parallel helps to expel destroyed cells from the body [17]. Moreover, whole grains are rich in antioxidants, including vitamins (like vitamin E), minerals and phenolic compounds, which have been reported to have anticancer properties [17,18]. Phytoestrogens, which can be found in whole grains, also have antioxidant properties, and are able to inhibit cell proliferation and angiogenesis and to induce apoptosis, especially in breast cancer [18].

Consumption of alcoholic drinks has been reported to increase the risk of cancer of the oral cavity and pharynx, larynx, and oesophagus, and to increase the risk of colorectal cancer, as well as of pre- and postmenopausal breast cancer [9,19]. The mechanisms by which alcohol consumption exerts its carcinogenic effects are various. Firstly, acetaldehyde, an alcohol metabolite, as well as producing free radicals, seems to have numerous carcinogenic properties, having also the ability to destroy DNA [20–22]. Furthermore, alcohol may take part in the transportation of carcinogenic substances in cells. Heavy drinking is linked with a low intake of nutrients, like folate, making the human body vulnerable to tumor pathogenesis [19,23]. Finally, concerning specifically breast cancer, alcohol consumption is reported to raise estrogen levels, which can induce carcinogenesis [22].

In October 2015, the cancer agency of the World Health Organization evaluated the carcinogenicity of red and processed meat. After reviewing the scientific literature, the experts classified the consumption of red meat as probably carcinogenic to humans while processed meat was classified as carcinogenic to humans [24]. That is in agreement with the existing guidelines for cancer survivors, which propose limited consumption of red and processed meat. The underlying mechanisms are already known. Red meat contains heme iron, a major source of stored body iron. Elevated body iron storage in humans has been shown to increase the risk of several cancers [25,26]. Moreover, processed meat can be a rich source of saturated fat. Fat intake in general has been hypothesized to increase the risk of overweight and obesity, which is itself a risk factor for some cancers [9]. Finally, during the processing and cooking of meat, substances added or formed like heterocyclic aromatic amines (HAA), N-nitroso compounds (NOC) as well polycyclic aromatic hydrocarbons (PAH), which seem to increase mammary tumors in animals and have been hypothesized to increase also cancer risk in humans [24,27–29].

3.2. Dietary supplements

The use of vitamin and mineral dietary supplements is widespread among cancer patients and long-term cancer survivors; indeed, individuals tend to increase their use of vitamin and mineral supplements after a diagnosis of cancer, often without their physician's knowledge. The term 'dietary supplement', according to the US Dietary Supplement Health and Education Act (DSHEA) of 1994, means a product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following dietary ingredients: a vitamin, a mineral, a herb or other botanical, an amino acid, a dietary substance for use by man to supplement the diet by increasing the total dietary intake or combination of any of the aforementioned [30]. According to the World Cancer Research Fund (WCRF)/American Institute for Cancer Research (AICR) report published in 2007, dietary supplements are not recommended for cancer prevention, since patients should aim to meet their individual needs through diet alone [9]. The Nutrition and Physical Activity Guidelines for Cancer Survivors published in 2012 by the American Cancer Society (ACS) seem to be consistent with the WCRF/

AICR recommendations. Indeed, the ACS proposes that all attempts should be made to obtain needed nutrients through dietary sources, and that supplements should be considered only if a nutrient deficiency is either biochemically or clinically demonstrated and if nutrient intakes fall persistently below two-thirds of the recommended intake [10]. The determination of such intake should be done by a registered dietitian, while the need for cooperation with health-care providers is obvious. Cancer survivors should be helped to understand that food is the best source of vitamins and minerals.

3.3. Body fat

In the last 3 decades there has been a worldwide increase in average body weight as well as in the prevalence of overweight and obesity, which itself is linked to an increased risk of chronic diseases like cardiovascular diseases and type 2 diabetes [31]. Moreover, according to the World Cancer Research Fund (WCRF)/American Institute for Cancer Research (AICR) report published in 2007, there is convincing evidence that excess body fat is a cause of adenocarcinoma of the oesophagus, and cancers of the pancreas, colorectum, breast (postmenopausal), endometrium, and kidney. Similarly, there is convincing evidence that excess abdominal (central) fat is a cause of colorectal cancer and it is probably also a cause of cancers of the pancreas, breast (postmenopausal), and endometrium [9]. Excess body fat is associated with increased concentrations of compounds that are known to increase cancer risk via mechanisms that involve cell proliferation, hormonal control as well as the immune system. For example, in postmenopausal women, adipose tissue is the predominant source of endogenous estrogens, whose increased circulating levels are linked with breast cancer risk [32]. Furthermore, excess body fat is associated with systemic inflammation and suppression of the immune system, which seems to be relevant to cancer [32]. Finally, hormones like insulin, leptin and insulin-like growth factor $_1$ (IGF $_1$) have been reported to have mitogenic and anti-apoptotic properties and as a result have been associated with many types of cancer [32]. In the light of the above mechanisms, the Panel as well as the American Cancer Society recommendations propose that individuals should strive to achieve and maintain a healthy weight, not only in order to prevent primary cancer but also its recurrence [9,10].

3.4. Physical activity

Due to urbanization and industrialization, people are increasingly leading sedentary lifestyles, a fact that probably has contributed to the increased prevalence of obesity as well as of chronic diseases like cardiovascular diseases, type 2 diabetes and even cancer. For this reason, physical activity could be an inexpensive and easily workable solution in our efforts to deal with these diseases. Physical activity firstly promotes weight management by reducing inflammation and improving the function of the immune system [33,34]. Moreover, it is positively associated with cardiorespiratory fitness, muscular strength and endurance, a fact that could be beneficial for cancer survivors and help them to regain their pre-treatment fitness and health [33,34]. Physical activity lowers the levels of hormones such as insulin and estrogen and of certain growth factors that have been associated with cancer development and progression. Finally, it is associated with significantly reduced fatigue and depression, and has significant effects on overall quality of life (QoL) in cancer survivors, by improving physical and psychological functioning [33,34].

The World Cancer Research Fund (WCRF)/American Institute for Cancer Research (AICR) as well as the American Cancer Society recommend that cancer survivors be moderately physically active, for at least 30 min each day, on five or more days of the week, so that, along with the appropriate dietary choices, they maintain a healthy weight and are protected against cancer recurrence [9,10].

Table 1

A summary of dietary and physical activity guidelines for cancer survivors.

Body fat	Be as lean as possible throughout life <ul style="list-style-type: none"> ● If currently overweight and obese, achieve and maintain a healthy weight ● Maintain body weight through adulthood within the normal range ● Avoid weight gain throughout adulthood
Physical Activity	Adopt a physically active lifestyle <ul style="list-style-type: none"> ● Limit sedentary habits and time spent in front of screens ● Engage in moderate physical activity for at least 30 minutes each day ● Engage in vigorous physical activity for at least 30 minutes each day when fitness improves
Nutrition	Adopt a healthy diet with an emphasis on plant-based foods <ul style="list-style-type: none"> ● Eat at least five portions/servings of a variety of vegetables and fruit every day ● Eat whole grains with every meal instead of processed (refined) grains ● Limit consumption of red meat (consume less than 500 g a week) and processed meat ● Limit consumption of energy-dense and fast foods ● Avoid sugary drinks ● Limit consumption of salt ● If alcoholic beverages are consumed, limit consumption to no more than two drinks/day for men and one drink/day for women

4. Conclusions and future directions

The incidence of new cancer cases is not expected to fall over the next few years, and the number of cancer survivors is increasing. There is a need to optimize nutrition after cancer, possibly with nutritional interventions, and to increase levels of physical activity. These are two of the few modifiable, ubiquitous factors relevant to cancer risk reduction. Table 1 summarizes the current scientific evidence regarding the association between nutrition and cancer survivorship, based on a thorough review of the guidelines. There is a need for well-designed large observational and intervention studies to shed more light on the association between diet and cancer survivorship, and to suggest additional means for the secondary prevention of cancer.

Contributors

NM wrote the first draft of the review.
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 EAK reviewed and revised the manuscript.
 KNS reviewed and revised the manuscript.
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Conflict of interest

The authors declare that they have no conflict of interest.

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