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Review Article

Lifestyles and Their Impact on Cancer

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Abstract: Cancer is a common disease and is growing in incidence and prevalence. It is expected to become the number one killer of humans in the coming decade. It is associated with considerable suffering, decreased survival, and huge economic costs. Death is usually due to metastasis. Major cancers include those of the lung, breast, colorectum, prostate, stomach, and liver. It results from a complex interaction involving genetic, environmental, and lifestyle factors. It is estimated that up to 95% of cancer events are attributable to lifestyle factors such as physical inactivity, cigarette smoking, poor diet, alcohol, and obesity. Smoking cigarettes is a major cause and may be responsible for 40% of all cancer cases in the US. Obesity is the next major modifiable lifestyle factor. The impact of improper diet and alcohol intake is estimated at being more than 5% followed by lack of physical activity. These factors are modifiable and can greatly help reduce the risk of common cancers, improve their management, and beneficially affect their prognosis. In addition, following healthy lifestyles will help mitigate the deleterious effects of many co-morbid chronic diseases that cancer patients have. This manuscript discusses the impact of these major lifestyles on cancer.

Keywords: Cancer, smoking, lifestyles, exercise, alcohol, diet, obesity.

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INTRODUCTION

Cancer is a common disease [1]. It is estimated that 1 in 5 men and 1 in 6 women developed cancer in 2016 [1]. According to the GLOBOCAN estimates, in 2018 there were 18.1 million new cases of cancer and it contributed to the death of 9.6 million people [2]. Cancer-related mortality exceeds that caused by communicable diseases such as human immunodeficiency virus/acquired immunodeficiency syndrome, tuberculosis, and malaria, combined [3]. The most common global cancers are those of the lung, colorectum, stomach, and liver [1]. Cancer prevalence is rising [4]. It is presently the second most common cause of death worldwide, second only to cardiovascular diseases (CVD), but is expected to become number one in the coming years [5]. It is estimated that the global burden of neoplasms is going to rise by more than half by the year 2040 [6].

DISCUSSION

Five lifestyles have been recognized as having a major impact on morbidity and mortality [7]. These behaviors are non-smoking, abstinence or low to moderate alcohol intake, a normal body mass index, regular exercise, and a prudent quality of diet [7]. According to Yanping *et al*., adherence to these lifestyles improves survival [7]. Lifestyles also play an important role in all aspects of most cancers [8, 9]. It is estimated that up to more than 90% of cancers are attributable to modifiable risk factors such as tobacco smoking, excessive body weight, physical inactivity, alcohol consumption, infectious agents, environmental pollution, and suboptimal diet [8, 9]. Smoking is the most harmful and is estimated to cause almost 30% of all cancers [[10]. Other modifiable behaviors may be responsible for another one-third of cancers - diet 5-10%, alcohol intake (4%–6%), excessive body weight (7%–8%), and physical inactivity (2%–3%) [11-13].

Smoking

There are about 1.1 billion smokers worldwide (21% of the world's population) aged 15 years and older [14]. Smoking is deadly and kills predominantly by causing lung cancer, chronic obstructive pulmonary disease, and myocardial infarction [15, 16]. It also causes or contributes to the development of a wide range of communicable and other non-communicable disorders [15, 16]. The average loss of life, compared with never-smokers, is 10–15 years [17, 18]. Smokers develop diseases such as cardiovascular disease, stroke,

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and dementia approximately 10 years earlier than non-smokers [17, 18].

Tobacco smoke is full of carcinogens [12, 19]. It is estimated that 40 percent of all cancers diagnosed in the United States are associated with smoking [20]. Smoking has been associated with cancer of almost every organ of the human body. It is estimated that smoking accounts for 81.7% of lung cancers, 73.8% of larynx cancers, 50% of esophageal cancers, 46.9% of bladder cancers and is responsible for 28.8% of all cancer deaths [12]. Other methods of smoking tobacco, such as water pipe smoking [21], Electronic Nicotine Delivery System smoking [21], and Heat-not-Burn smoking [22] have also been implicated in increasing the cancer risk. Second-hand smoke also increases the risk of cancer [23]. Smokeless tobacco also poses a risk, causing cancers of the oral cavity, esophagus, and pancreas [24].

Approximately 1 in 3 patients are active smokers at or around the time of cancer diagnosis [25]. Smoking tends to reduce treatment effectiveness [26], increase the likelihood of recurrence [27], or promote the development of new primary tumors [28] in these patients. Overall, continued smoking after cancer diagnosis indicates a poor prognosis and a deteriorating quality of life as compared with cancer patients who quit [29]. Smokers with a cancer diagnosis also suffer from an increased mortality [25]. The mortality risk is reduced by 30% to 40% with smoking cessation [30]. Overall, smoking cessation after a cancer diagnosis has benefits that equal or exceed those achieved by cancer treatments [31]. Quitting smoking also helps in mitigating several comorbid chronic diseases that are often present in these patients [32, 33].

Alcohol

Alcohol consumption is common worldwide [34]. It is beneficial for several diseases – so long it is consumed in low to moderate amounts [35, 36]. However, alcohol abuse can also result in liver and gastrointestinal problems, cognitive defects, peripheral neuropathy, and psychological disorders [37]. Heavy alcohol intake is also detrimental for diabetes and cardiovascular diseases [38, 39].

Alcohol is a known carcinogen [40-43]. It is responsible for 6.4% of all cancers in women and 4.8% of all cancers in men12. Esophageal cancer has the strongest association with alcohol intake[44]. Breast tissue is extremely susceptible to alcohol intake [45] and there is a 7–10% increase in risk for each 10 g (~1 drink) alcohol consumed daily by adult women irrespective of their menopausal state [46]. It is estimated that alcohol consumption is responsible for 4–10% of breast cancers in the USA [47]. Binge drinkers increase their risk even more – by 21%, according to the Nurses' Health Study [48]. Alcohol intake has also been linked with an increase in other cancers [49]. These include gastric cancer [50], colo-rectal cancer [51], liver cancer [52], prostate cancer [53], lung cancer [52], and some skin cancers [54]. It also increases the risk of a second aerodigestive-tract cancer [55]. In a review of 222 articles in 2013, (comprising of about 92 000 light drinkers and 60 000 non-drinkers with cancer) Bagnardi and group found that light drinking increases the risk of oropharyngeal cancer by 17%, esophageal squamous cell carcinoma by 30%, and breast cancer by 5% [56]. In a more recent review, using data published by the International Agency for Research on Cancer and the World Cancer Research Fund/American Institute for Cancer Research, Islami *et al*., found that alcohol intake was responsible for an estimated 40.9% of oral cavity/pharynx cancers, 23.2% of larynx cancers, 21.6% of liver cancers, 21% of esophageal cancers, and 12.8% of colorectal cancers12. Alcohol intake is responsible for 4.0% of all cancer deaths [12].

There appears to be no safe limit of alcohol intake when it comes to cancer. Even small amounts of alcohol intake are carcinogenic. There appears to be a dose-related association between alcohol intake and cancer. Cancer mortality among current light, moderate, heavy, and very heavy drinkers had a Hazard Ratio of 1.58, 2.28, 2.34, and 2.97 respectively. The highest risk of cancer mortality was observed in former drinkers, who demonstrated a Hazard Ratio of 3.86 [57]. Acetaldehyde, the main metabolite of alcohol is a carcinogen [45, 58]. It also acts as an irritant to the upper GI tract [59]. Its intake is associated with abnormal production of reactive oxygen and nitrogen species, aberrant DNA methylation and repair, disturbed immune surveillance and inflammatory response, and increased estrogen levels in breast cancer cases [60]. Other mechanisms noted include increased levels of plasma insulin-like growth factors produced by the liver following alcohol consumption, alcohol acting as a solvent for tobacco carcinogens, alcohol-related lesions that favor the absorption of carcinogens in the aerodigestive tract epithelium, and changes in folate metabolism [61], Ethanol might also be immunosuppressive, thereby enhancing or facilitating carcinogenesis in various organs [52, 62]. In addition, carcinogenic contaminants can be introduced during alcoholic beverage production [63].

Obesity

BMI is widely used as a measure to define body weight [64]. BMI is categorized into several groups: < 18.5 kg/m^2 (underweight), 18.5–24.9 kg/m^2 (normal weight), and 25 to 29.9 kg/m^2, (overweight). Obesity is defined as a BMI exceeding 30 kg/m^2 and is subclassified into class 1 (30–34.9), class 2 (35–39.9), and class 3 or severe obesity (≥ 40). A BMI >50 Kg/m2 is considered morbid obesity [65]. Central obesity can be objectively ascertained by several anthropometric measurements, including waist circumference (<102 cm in males and <88 cm in females), waist to hip ratio (normal: 0.85 or less for women and 0.9 or less for

men), and the waist-height ratio (< 0.5 indicates no visceral obesity and ≥ 0.5 is consistent with visceral obesity) [66-69]. Obesity underlies conditions such as cardiovascular disease, hypertension, diabetes mellitus, nonalcoholic fatty liver disease (NAFLD), gallbladder disease, pancreatitis, sleep apnea, and osteoarthritis [70]. It also increases the risk of cancer [71-75]. Visceral obesity appears to be more pro-oncogenic than BMI [76].

According to a recent report by the International Agency for Research on Cancer (IARC), which analyzed more than 1000 epidemiological studies, there is sufficient evidence to classify obesity, measured by body mass index (BMI), as a causal cause for 13 types of cancers75. These include cancer of the esophagus [77], liver [78], gallbladder [79], pancreas [80], breast [81], stomach [82], uterus [83], ovary [84], kidney [85], colon/rectum [86], and meninges [87]. Males are more prone to an increased risk for neoplasms of the colon, rectum, and prostate while women have an increased risk for cancers of the breast, endometrium, and gallbladder [88, 89].

In 2018, 67% of cancer survivors in the US were overweight or obese [90]. Obese patients with cancer do not thrive well. Several studies have documented treatment-related toxicity in obese children and obese adults [89, 91]. Obesity often results in an increase in cancer recurrence, cancer progression, and a negative prognosis in survivors [92]. It also reduces the quality of life in cancer survivors [93]. Obese survivors of many obesity-related cancers also have an elevated risk of developing second primary cancers [94]. Obese cancer patients also experience a high mortality rate [95]. Among patients with a BMI ≥40 kg/m^2 compared with patients with a normal BMI, mortality from all causes of cancer was found to be 52% higher in men and 62% higher in women [70]. It is estimated that obesity-related cancer deaths in men and women combined account for 6.5% of all cancer deaths12. Visceral or central obesity is associated with worse cancer outcomes [96]. Further, more than 40% of the patients diagnosed with cancer also have comorbid diseases, such as diabetes, chronic obstructive pulmonary disease, heart failure, and coronary artery disease – and obesity is detrimental to these conditions as well [97].

Potential biologic mechanisms include increased levels of endogenous hormones (sex steroids, insulin, and insulin-like growth factor I) associated with overweight and obesity and the contribution of abdominal obesity to gastroesophageal reflux and esophageal adenocarcinoma [98]. Obesity contributes to a pro-carcinogenic environment by initiating several sex and growth hormonal changes, producing pro-inflammatory states (which can cause DNA damage), increased blood levels of insulin, and insulin-like growth factor-1 (IGF-1), promoting oxidative stress, cell proliferation and angiogenesis, and inhibition of apoptosis/cell death [93, 94, 99]. Altered gut microbiome with obesity may also play a role [100]. Other mechanisms may also play a role [101].

Exercise

One MET equals an energy expenditure of 1 kcal/kg/hour or an oxygen uptake of 3.5 ml/kg/min [102]. Physical activity is defined as any bodily movement produced by skeletal muscles that result in energy expenditure [103]. Sedentary behavior is defined as any waking behavior characterized by an energy expenditure ≤1.5 metabolic equivalents [104] (such as TV viewing, video game playing, computer use, driving or riding in a car, and reading/studying while sitting) [105]. This behavior is associated with obesity [106] and a higher incidence of cardiovascular disease, type 2 diabetes, and cancer [107-109]. Exercise is a subcategory of physical activity and is planned, repetitive, and purposive [110]. Exercise is commonly classified according to the metabolic equivalent (MET) expended. Light-intensity activities expend less than 3 METs, moderate-intensity activities expend 3 to 6 METs, and vigorous activities expend 6 or more METs [111].

According to Islami *et al*., physical inactivity accounted for 2.9% of all cancer cases in the US [12]. They estimated that physical inactivity accounted for 26.7% of uterine cancers, 16.3% of colorectal cancers, and 3.9% of female breast cancers [12]. A recent umbrella review, including 19 reviews, 26 meta-analyses, and 541 original studies, evaluating physical activity and cancer risk, concluded that regular physical activity is beneficial in preventing 7 major cancers (colon, breast, endometrium, lung, esophagus, pancreas, and meningioma) [112]. Several studies have also reported significant reductions in physical activity in cancers of stomach, kidney, bladder, and endometrium [113-115]. In another more recent study, exercising 7 hours a week reduced colon cancer risk by 40% [116]. Individuals exercising before a cancer diagnosis do better [117, 118]. Exercise helps them with better coping with common cancer-related health problems, including emotional distress, fatigue, and diminished physical functioning [119-121]. During treatment, it improves interventional effectiveness and diminishes side effects [121-123]. Exercise also helps prevent cancer recurrence, both local and distant [124, 125]. The overall quality of life (QOL) improves [126], and cancer-related mortality is reduced [127, 128]. Regular exercise is recommended by various world health organizations for cancer patients [129]. Exercise benefits in cancer; also extend to coexisting NCDs More than 40% of the patients diagnosed with cancer have comorbid NCDs, such as diabetes, obesity, chronic obstructive pulmonary disease, and heart failure [130]. Cancer itself may increase the risk of developing some of these diseases [131]. Physical activity induces several cancer-preventive changes in the human body,

including reducing adipose tissue, improving insulin resistance, reducing inflammation, enhancing immune function, modulating sex hormones and growth factors, and enhancing resistance to oxidative stress and DNA damage [132,133]. In patients with established malignant tumors, physical activity/exercise paradigms regulate intra-tumoral vascular maturity and perfusion, hypoxia, and metabolism and augment the antitumor immune response [134].

Diet

Diet plays an important role in cancer [135-137]. In 2015, more than 80 000 new cancer cases among US adults were associated with suboptimal dietary intake [138]. These included cancers of the colon and rectum, followed by cancer of the mouth, pharynx, and larynx; corpus uteri, breast (postmenopausal), kidney; stomach; liver, pancreas, esophagus (adenocarcinoma), thyroid, prostate (advanced), multiple myeloma, ovary, and gallbladder [138].

The benefits of a plant-based diet on cancer are well established [139]. In a review of 206 human epidemiologic studies and 22 animal studies, Steinmetz and Potter found that greater vegetable and fruit consumption is preventive for cancers of the stomach, esophagus, lung, oral cavity and pharynx, endometrium, pancreas, and colon [140]. Donaldson estimated that plant-based eating patterns can reduce the risk of breast cancer, colorectal cancer, and prostate cancer by 60–70% and lung cancer by 40–50% [141]. On the other hand, a 200 g/day decrease in fruit and non-starchy vegetable consumption is associated with a risk increase of 2% for colorectal cancer and a 9% increase in the risk of lung cancer [142]. Islami *et al*. recently reported that low fruit and vegetable intake accounted for 1.9% of all cancer cases [12]. This group also found that low fruit and vegetable consumption was implicated in the development of 17.6% of oral cavity/pharyngeal cancers, 17.4% of laryngeal cancers, and 8.9% of lung cancers while low dietary fiber accounted for 10.3% of colorectal cancer cases [143]. A diet rich in meat and animal products has been shown to increase cancer incidence, especially cancers of the breast, colon, stomach, and prostate [144-146]. According to Islami et al. red meat consumption was associated with 5.4% of colorectal cancers [12]. Processed meat intake is especially harmful, with data suggesting the cancer risk was 16%-18% higher for each 50 g/day increments in intake [147]. It has been estimated that processed meat consumption is associated with 8.2% of colorectal cancers [12]. The study by Zhang *et al.* indicated that insufficient whole-grain intake accounted for the largest number and proportion of cancer cases in 2015 (1.8%), followed by insufficient dairy intake (1.2%); high processed meat intake (1.0%); insufficient vegetable intake (0.8%); insufficient fruit intake (0.5%); high red meat intake (0.4%); and high SSB intake (0.2%) [138].

A proper diet also helps reduce several associated symptoms of cancer and helps improve the quality of life in these individuals [148]. They also benefit from an improved survival [149, 150]. Cancer survivors are at an increased risk of secondary cancers [151, 152], and a plant-based diet has also been shown to retard the development of secondary cancers153. Mediterranean diet, a diet that is predominantly plant-based and incorporates olive oil and a glass or so of red wine with meals, is inversely associated with the risk of developing colorectal, head and neck, respiratory, gastric, liver and bladder cancer as well as cancer mortality, and all-cause mortality among cancer survivors [154].

There are several mechanisms by which low intakes of red meat, processed meat, and salt and high intakes of dietary fiber, fruit, and non-starchy vegetables may contribute to the prophylactic and therapeutic effects noted in cancer [155-158]. These include decreased exposure to carcinogens including N-nitroso compounds, decreased formation of cyto- and genotoxic aldehydes, reduced inflammation, enhanced antioxidative capacity, improved DNA repair, reductions in adipose tissue, decreased insulin levels, improved levels of circulating sex and growth hormones. and the formation of heterocyclic aromatic amines and polycyclic aromatic hydrocarbons during high heat cooking of meat [155,156]. Vegetables diversify gut microbiomes, resulting in lower inflammation, better immunity, decreased tumorigenesis, and potentiation of the immunotherapeutic effects in cancer treatment and prevention157. Acrylamide, a chemical produced during high-temperature cooking, a process involved in the production of potato chips, is probably carcinogenic to humans [158].

Cancer survivors are also at an increased risk of chronic ailments such as diabetes, osteoporosis, and cardiovascular disease [159,160]. A proper diet will help beneficially modify these risks. Plant-based diets may also reduce obesity, another factor negatively associated with cancer [161,162].

CONCLUSION

Cancer is a dreaded disease. There were an estimated 19.3 million new cases of cancer diagnosed globally in 2020 (www.iarc.who.int). For both sexes combined, the top 10 cancer types account for >60% of the newly diagnosed cancer cases and >70% of the cancer deaths. It is estimated that the global burden of cancer is going to continue to rise over the next few decades. Cancer has become a big barrier to the quest to increase longevity. Most cancers arise from a complex etiology involving genetic, environmental, and lifestyle factors. Major lifestyle factors include smoking, alcohol intake, exercise, obesity, and diet. They play an important in the genesis and progression of most cancers. Healthy lifestyles not only prevent cancer, but

also decrease the progression of cancer, allow better response to treatment, mitigate side effects of treatment, improve the quality of life, and reduce mortality. They also help reduce the impact of several chronic diseases that often c0-exist in these patients.

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