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OPTIMIZING LIFESTYLE REDUCES THE RISK OF CANCER IN DIABETES

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Diabetes mellitus has been epidemiologically associated with an increased risk of cancer. The results of several studies indicate that the relative risks are greatest for cancers of the liver, pancreas, and endometrium, and lesser for cancers of the colon and rectum, breast, and bladder. Several potential factors present in diabetic patients, like: obesity, quality of metabolic control, increased oxidative stress, inflammatory cytokines, may influence the association between diabetes and cancer. Several studies indicate that optimizing lifestyle (dietary interventions, physical activity, cessation of smoking) reduce the risk of cancer associated with diabetes. Epidemiologic studies consistently show that several cancers are diet related and changes of diet may decrease the risk to developing this condition. The following anti-cancer diet greatly lowers the risk of colorectal cancer and nearly all other types of cancers: low in total fat and very low in saturated fats, rich in fibers and fruit, vegetables, and grain products. Physical activity is associated with a lower risk of colon, postmenopausal breast, and endometrial cancer and may improve cancer survival. Physical activity may protect against cancer and tumor development through its role in energy balance, hormone metabolism, by decreasing the time of exposure to potential carcinogens, and by decreasing the inflammatory and immune factors, some of which may influence cancer risk.

Key words: diabetes mellitus, cancer, risk factors.

INTRODUCTION

Diabetes and cancer are common diseases that have a great impact on health worldwide. Epidemiologic evidence suggests that people with diabetes are at a significantly higher risk of many types of cancers. The relative risks are greatest (about twofold or higher) for cancers of the endometrium, pancreas, and liver, and lesser (about 1.2–1.5 fold) for cancers of the breast, colon and rectum, bladder. For other cancer sites, there appears to be no association or the evidence is inconclusive[1,2,3,4,5].

The American Diabetes Association and the American Cancer Society convened a consensus development conference in December 2009. After a series of scientific presentations by experts in the field, the writing group independently developed a consensus report published in July 2010. Data collected from experts reported that: "Evidence from observational epidemiologic studies consistently shows that higher levels of physical activity are associated with a lower risk of colon, postmenopausal breast, and endometrial cancer. Physical activity may also help prevent other cancers, including lung and aggressive prostate cancer, but a clear link has not been established. Some evidence also suggests that physical activity postdiagnosis may improve cancer survival for some cancers, including breast and colorectal. A protective role for increased physical activity in diabetes metabolism and outcomes has been demonstrated. Data from observational and randomized trials suggest that ~30 min of moderate-

intensity exercise, such as walking, at least 5 days per week substantially reduces (25–36%) the risk of developing type 2 diabetes"[5].

FACTORS THAT MAY INFLUENCE THE RISK OF CANCER IN DIABETES

Nonmodifiable risk factors

Age.The prevalence of diabetes mellitus and of most cancers increases with age. The relationship between cancer and aging is unclear. During normal ageing cells accumulate damage and stress-dependent changes. The pre-malignant tumour cells rapidly accumulate damage, in part owing to the presence of oncogenes, leading to a higher proportion of tumour cells becoming senescent. Tumour progression to full malignancy is favoured when tumour cells acquire mutations that impair the senescence program[6]. The biological process of ageing contributes to increased risk of diabetes and the National Health and Nutrition Examination Survey (NHANES III) demonstrated that, in the population over 65 years old, almost 18% to 20% have diabetes[7].

Sex. Certain cancers are sex-specific but overall cancer occurs more frequently in men[5].

Modifiable risk factors

Obesity. According to the American Cancer Society, and Obesity Society, obesity increases the risk of cancers but the relationship between obesity and cancer is not fully understood[8,9]. Obesity is characterized by increased of estrogen levels (by peripheral conversion of androstenendione in adipose tissue), insulin resistance and hyperinsulinemia, altered production of adipokines, that may be important contributors to the increased risk for cancer development and progression[10,11,12].

Diet. Several studies indicating that the dietary patterns, are closely associated with the risk for several types of cancer.

Physical activity. A literature review identified several studies that found statistically significant, positive associations between sedentary behaviour and cancer outcomes. Sedentary behaviour was associated with increased colorectal, endometrial, ovarian, and prostate cancer risk. The association between sedentary behaviour and cancer supported the hypothesized role of adiposity and metabolic dysfunction in the pathogenesis of cancer[13].

*Tobacco sm*oking. Tobacco smoking is associated with several types of cancer like trachea, bronchus, lung, larynx, liver, stomach, and uterine cervix cancers[5].

Alcohol. Alcohol is associated with an increased risk of a number of cancers (mouth, oesophagus, pharynx, larynx, colorectal, liver, stomach, breast and ovaries). Increased acetaldehyde production via alcohol dehydrogenase has been implicated in the pathogenesis. A study of 818 heavy drinkers found that those who are exposed to more acetaldehyde than normal through a defect in the gene for alcohol dehydrogenase are at greater risk of developing cancers[14]. In 1988 the International Agency for Research on Cancer of the World Health Organization has classified alcohol as a group 1 carcinogen[15].

Interactions between diabetes and cancer

Hyperglycemia. The association of hyperglycaemia with total cancer risk, independent of obesity, provides further evidence for an association between abnormal glucose metabolism and cancer. The researchers recommended a lifestyle that decreases plasma glucose levels and this may reduce overall cancer risk not only among overweight but most likely also among subjects with normal body weight[16].

Increased oxidative stress. Oxidative stress is caused by the presence of reactive oxygen species which the cell is unable to counterbalance. The result is damage to biomolecules including deoxyribonucleic and ribonucleic acid, proteins and lipids. Several studies indicating that oxidative stress has been implicated in the natural aging process as well as a variety of neoplastic, diseases. Oxygen-free radicals may act within cells as secondary messengers in intracellular signalling cascades, which induce and maintain the oncogenic phenotype of cancer cells[17,18,19].

Diabetes treatments. The current recommenddations regarding the metabolic control in diabetic patients impose the administration of supraphysiological insulin doses. Insulin and insulin analogues have metabolic and mitogenic activities in the cell. It is an important distinction between mitogenity and carcinogenicity, which refers to the ability or tendency to transform cells and promote tumor growth[20]. Large, prospective. randomized clinical trial with a lengthy follow-up period are necessary to establish that insulin displays carcinogenic behaviour.

THE ROLE OF OPTIMIZING LIFESTYLE IN DECREASING THE RISK OF CANCER ASSOCIATED WITH DIABETES

The American Cancer Society published in 2006 Nutrition and Physical Activity Guidelines to serve as foundation for strategies, to affect dietary and physical activity patterns among Americans. These guidelines, published every 5 years, are developed by a national panel of experts in cancer research, prevention, epidemiology and public health. The Guidelines emphasize the importance of maintaining a healthy body weight. The way to achieve a healthy body weight is to balance energy intake (food and beverage intake) with energy expenditure (physical activity). Caloric intake can be reduced by decreasing the size of food portions and limiting the intake of foods and beverages that are high in calories, fat, and/or refined sugars. The Guidelines recommend that these foods and beverages should be replaced with choices like vegetables and fruits, whole grains, beans, and lowcalorie beverages[21].

The results of European Prospective Investigation into Cancer and Nutrition recommend the following anti-cancer diet that greatly lowers the risk of colorectal cancer and nearly all other types of cancers: diet low in total fat and very low in saturated fats, high fiber diet (fiber moves potential carcinogens through the intestines faster, decreasing the contact time between carcinogens and the intestinal wall), and high fruit, vegetable, and grain products diet[22].

Scientific evidence indicates that physical activity is associated with a lower risk of colon, postmenopausal breast, and endometrial cancer[5]. The Guidelines of American Cancer Society recommend adopting a physically active lifestyle: “adults: engage in at least 30 minutes of moderate to vigorous physical activity, above usual activities, on 5 or more days of the week, 45 to 60 minutes of intentional physical activity are preferable, children and adolescents: engage in at least 60 minutes per day of moderate to vigorous physical activity at least 5 days per week”[21].

Physical activity acts in a variety of mechanisms to reduce cancer risk: regular and intentional physical activity helps maintain a healthy body weight by balancing caloric intake with energy expenditure, through its role in energy balance, hormone metabolism and by decreasing the time of exposure to potential carcinogens. Physical activity has also been found to alter a number of inflammatory and immune factors, some of which may influence cancer risk. Physical activity may reduce proinflammatory factors, such as C-reactive protein, interleukin-6, and tumor necrosis factor-α. The immune system plays a role in reducing cancer risk by recognition and elimination of abnormal cells or through immune system components-acquired, innate, or both. The effects of moderate-intensity physical activity result in enhanced immune function, whereas exhaustive exercise, or high-intensity exercise may lead to immunosuppression, such as increased susceptibility to infections[23].

Types of Activity. The optimal intensity, duration, and frequency of physical activity needed to reduce cancer risk are unknown but evidence suggests that at least 30 minutes of moderate to vigorous activity, in addition to usual activities throughout the day, can help reduce cancer risk. To reduce risk of cancers of the colon and breast, evidence suggests that 45 to 60 minutes on 5 or more days of the week[21]. Usual activities are typically of low intensity and short duration. Moderate activities are those that require effort equivalent to a brisk walk and vigorous activities generally engage large muscle groups and cause a noticeable increase in heart rate and frequency, and sweating. For people who are largely inactive and people with chronic illnesses and/or established cardiovascular risk factors should consult their physicians before beginning a vigorous physical activity program. Examples of moderate and vigorous activities: walking, dancing, leisurely bicycling, canoeing, yoga, volleyball, golfing, softball, baseball, badminton, doubles tennis, garden maintenance (moderate intensity activities) and jogging, running, fast bicycling, circuit weight training, aerobic dance, martial arts, manual labour such as forestry (construction vigorous intensity activities)[21].

Increasing the level of physical activity at any age may reduce the risk of some cancers. Physical activity plays an important role in children's and adolescents' health and has important physical, mental, and social benefits. The American Cancer Society recommends: children and adolescents should be encouraged to be physically active at moderate to vigorous intensities for at least 60 minutes per day on 5 or more days per week. Activities should be, enjoyable and varied including sports and fitness activities in school, at home, and in the community. The daily physical education programs and activity should be

provided for children at school, and television viewing and computer game time should be minimized at home[21].

Scientific evidence indicates that physical activity is associated with a lower risk of colon, postmenopausal breast, and endometrial cancer.

The relationship between physical activity and endometrial cancer. The results about 20 studies that have examined the role of physical activity on endometrial cancer risk suggest an inverse relationship between physical activity and endometrial cancer incidence. These studies suggest that women who are physically active have a 20 percent to 40 percent reduced risk of endometrial cancer[24]. Changes in body mass and changes in the levels and metabolism of sex hormones are the major biological mechanisms thought to explain the association between physical activity and endometrial cancer.

The relationship between physical activity and colorectal cancer. Colorectal cancer has been one of the most extensively studied cancers in relation to physical activity (more than 50 studies examining this association.). The results of these studies found that adults who increase their physical activity, can reduce their risk of developing colon cancer by 30 to 40 percent relative to those who are sedentary behaviour[24,25,26].

The relationship between physical activity and breast cancer. The relationship between physical activity and breast cancer incidence has been studied in over 60 studies. Most studies indicate that physically active women have a lower risk of developing breast cancer than inactive women. And the amount of risk reduction achieved through physical activity varies between 20 to 80 percent[24].

Physical activity may improve cancer survival for breast and colorectal cancers[5], but the protective association of physical activity after diagnosis and survival in other cancers is inconsistent[24].

CONCLUSIONS

Diabetes has been associated with increased risk of several of the more common cancers.

The potential factors present in diabetic patients (obesity, quality of metabolic control, increased oxidative stress, the potential role of inflammatory cytokines) may influence the association between diabetes and cancer.

Several studies indicate that optimizing lifestyle (dietary interventions, physical activity, cessation of smoking) reduces the risk of cancer in patients with diabetes.

The anti-cancer diet recommended by international guidelines and studies in this field include diet low in total fat and very low in saturated fats, high fiber diet and rich in fruits, vegetables, and grain products .

Regarding adopting a physically active lifestyle, it is recommended that adults engage in at least 30 minutes of moderate to vigorous physical activity, above usual activities, on 5 or more days of the week, forty-five to 60 minutes of intentional physical activity are preferable, whereas children and adolescents should engage in at least 60 minutes per day of moderate to vigorous physical activity at least 5 days per week.

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