

Exploring the Relationship between Glycemic Index (GI) and Cancer Risk

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Abstract: Obesity and unhealthy diet are important factors that cause cancer. Currently, the application of low GI diet in the prevention and control of diabetes has received increasing attention. A large number of studies have found that a high GI diet can lead to changes in blood sugar and insulin levels, and is one of the important causes of diabetes, tumors, and cardiovascular diseases. Existing studies have shown that there is a close connection between diabetes and cancer, but there are few reports on the relevant mechanisms and risk factors for dietary GI induced cancer. A literature search found that high GI foods increase the incidence of cancer, but there are no large number of experiments to prove whether a low GI diet improves the occurrence of cancer. Therefore, this article proposes and explains the hypothesis of the relationship between glycemic index (GI) and cancer risk, providing new research ideas for the prevention of cancer with a low GI diet.

Keywords: Glycemic Index; Cancer; Low GI Diet.

1. Research Background

In recent years, with the rapid development of the national economy, people's material living standards have gradually improved, and people's awareness of dietary nutrition and health has been strengthened. People's nutritional status and nutritional needs have undergone tremendous changes, and the fundamental reason lies in the changes in lifestyle and diet. Some studies have shown that the correlation between dietary structure and chronic metabolic diseases is increasing [1]. The "Report on the Nutrition and Chronic Disease Status of Chinese Residents" shows that the incidence of diabetes in people aged 18 and above in China reached 9.7% in 2012 [2], and rose to 11.9% in 2020, with type 2 diabetes accounting for more than 90% [3]. Severe diabetes can also cause related complications, such as kidney disease, heart disease, and tumors [4]. Long-term high blood sugar levels are closely related to the GI value of food and glycemic load [5]. Therefore, the glycemic index (GI) is an effective indicator for evaluating the reaction of blood sugar changes after carbohydrates enter the body. A low GI diet is not only effective in controlling blood sugar, but also can improve the blood lipid status and insulin action of obese people [6].

China is not only the country with the highest number of diabetes patients, but also one of the countries with the highest cancer incidence rates[7]. Obesity and unhealthy diet are considered to be one of the main risk factors for malignant tumors, with a high mortality rate, such as common endometrial cancer, colon cancer, breast cancer, etc.[8]. Cancer cells use glucose absorption, transport and glycolysis as their main energy source, leading to abnormal cell metabolism[9]. In recent years, the role of dietary intervention in tumor prevention and treatment has received attention at home and abroad, such as the ketogenic diet and the Mediterranean diet[10],[11]. The low GI diet has been used in the dietary management guidance of diabetic patients[12], but the research on the low GI diet and cancer is still in the exploratory stage.

The global study of GI diet has lasted for half a century, and some countries have used the GI value of food as a nutritional indicator in the food processing process [12]. At present, there is little research on the effect of dietary GI on the cause of cancer, and there is controversy over whether a low GI diet can reduce the incidence of cancer.

This article studies the glycemic index (GI) and the predisposing factors of various cancers, and explores the application value of a low GI diet in cancer prevention and treatment, aiming to provide new ideas for the use of low GI foods in cancer prevention and treatment.

2. Overview of Glycemic Index (GI)

The glycemic index (GI) was first proposed by Canadian nutrition professor Dr. David Jenkins in 1981[13]. The Food and Agriculture Organization (FAO)/World Health Organization (WHO) defines GI as the blood glucose response curve (AUC) of a food containing 50 grams of carbohydrates and the blood glucose response rate of an equal dose of food within a certain period of time (such as 2 hours). It is also an important indicator for evaluating postprandial blood glucose levels after food intake[14]. Foods with a GI value below 55 are low-GI foods. Compared with medium-GI and high-GI foods, low-GI foods stay in the gastrointestinal tract longer, reducing the absorption rate of the small intestine and the peak of blood glucose fluctuations[15]. The GI value of food is affected by many uncontrollable factors and is related to food processing methods and food types. Studies have shown that a low-GI diet has therapeutic significance for improving postprandial hyperglycemia and insulin resistance[16],[17]. In recent years, food GI has been widely used in dietary nutrition guidance as a scientific basis for food selection for people with specific needs[12].

3. Cancer Overview

Data recently released by the World Health Organization

show that China had 4.57 million new cancer patients in 2020, accounting for about 23.7% of the world's total[18]. China's cancer incidence and mortality rates rank first in the world, and the burden of cancer has continued to increase in recent years, posing a serious threat to human health[18]. Disturbance of glucose metabolism is one of the common characteristics of cancer. Cancer patients often experience a series of clinical manifestations such as anorexia, vomiting, and weight loss during the course of the disease. These symptoms are all caused by metabolic disorders or malnutrition. At present, most cancer patients use nutritional therapy for recovery, but the preventive and therapeutic effects of a low GI diet on cancer patients have not been fully studied and confirmed.

4. Glycemic Index (GI) and Cancer Overview

Currently, there are few studies on the relationship between food GI and cancer at home and abroad. Studies have confirmed the intervention effect of low GI diet on diabetes [19]. When high-sugar foods are ingested into the body, postprandial blood sugar rises, fat accumulates, and insulin resistance occurs. The intake, processing methods, and supply of other nutrients of CHO can cause changes in blood insulin and blood sugar [20], [21]. Compared with low GI foods, high GI foods are more likely to cause blood sugar rises and insulin changes, leading to glucose intolerance, insulin resistance, and hyperinsulinemia. Studies have found that both high GI and high GL diets can lead to insulin resistance and hyperinsulinemia, thereby promoting the occurrence of diseases such as diabetes and tumors [22]. The "Guidelines for Tumor-Related Management" (2021) point out that high blood sugar and diabetes increase the incidence of malignant tumors and high mortality. In cancer patients, persistent high blood sugar levels increase the patient's chance of postoperative infection and also increase pain [23]. Hyperglycemia, insulin resistance, diabetes, and diseases related to blood sugar metabolism can affect the division, reproduction, and metastasis of cancer cells [24], [25]. Insulin is a hormone that controls blood sugar. Its main function is to promote the synthesis of fat and protein and inhibit their decomposition. Cancer cell proliferation and metastasis may also be caused by the increase in the biological activity of insulin growth factor (IGF), IGF binding protein (IGFBPs), and IGF-I when the effect of insulin in regulating blood sugar is weakened, thereby inhibiting cell apoptosis [26]. Recently, a report in *The Lancet Diabetes and Endocrinology* pointed out that the intake of high GI foods increases the incidence of type 2 diabetes, cardiovascular disease, and cancer. The intake of dietary fiber and grains in food is closely related to a low GI diet, and diabetes-related cancer lesions may occur [27].

4.1. Diabetes-related Cancers

The 2023 "Chinese Adult Diabetes Expert Consensus" conducted in-depth research and predictions on diabetes. People with diabetes are more likely to develop complications such as cardiovascular and cerebrovascular diseases and tumors. There are many factors that induce diabetes-related cancers, including metabolic changes such as hyperglycemia, insulin resistance, and hyperinsulinemia, which can promote the formation of cancer cells. Cancer cells increase their proliferation, division, and migration capabilities through

glucose uptake, while excessive glucose metabolism affects insulin secretion. Long-term poor blood sugar control and the intake of foods that increase blood sugar levels quickly can affect insulin sensitivity, inflammatory response, and immune function abnormalities, leading to the risk of cancer progression and high mortality. Currently, there is little evidence to support the causal relationship between hyperglycemia and cancer, and there is great controversy [28]. Research on sugar-control diets for cancer patients has gradually attracted people's attention, and more and more scholars have begun to study the significance of the GI value of food on blood sugar regulation. Studies have shown that a high GI diet can quickly promote insulin secretion, lead to reduced insulin sensitivity, and even induce diseases such as diabetes and cancer [29], [30], [31]. When a low GI diet is used, the rate of glucose absorption in the small intestine is reduced, which can effectively improve insulin sensitivity and gastrointestinal hormones, thereby achieving the goal of controlling and lowering blood sugar [32].

4.1.1. Colorectal Cancer

Colorectal cancer (CRC) is also one of the malignant tumors with a high incidence rate today. Dietary habits and alcohol are the main causes of CRC. The risk of diabetes-related colorectal cancer is increasing year by year, due to changes in blood sugar level and abnormal insulin secretion, which accelerates the division and proliferation of cancer cells[33]. At the same time, the content and type of carbohydrates in the diet are a potential factor in causing colon cancer. Foods with high starch content in carbohydrates, such as refined carbohydrates, and high-fat foods can accelerate small intestine absorption, while low GI foods are rich in dietary fiber and can promote intestinal peristalsis[34]. At present, there are few studies on the correlation between colorectal cancer and food GI values, and there is still a lack of strong evidence.

4.2. Hormone-related Cancers

Hormone is an active substance that plays an important regulatory role in the human body. Sex hormones regulate the maturation of sexual organs and maintain sexual function. Insulin disorders may also be caused by excessive secretion of sex hormones. In a population-controlled experiment, it was found that the glycemic index had no direct relationship with the incidence of ovarian cancer [35]. However, another article put forward the opposite view that there is a strong correlation between sex hormones and insulin. Changes in estrogen in premenopausal and postmenopausal women and a decrease in hormone levels lead to the activation of the IGF signaling pathway, which promotes cell division, proliferation and migration. The intake of carbohydrates and dietary fiber will affect the changes in women's estrogen levels and insulin resistance levels, which may be indirectly related to the induction of ovarian cancer [36]. Many studies have found that abnormal insulin levels increase the incidence of hormone-related cancers, such as laryngeal cancer, endometrial cancer, prostate cancer, thyroid cancer, etc. [37], [38]. A high GI diet contains a lot of carbohydrates, which will reduce insulin sensitivity, while causing inflammatory reactions and oxidative stress reactions, causing changes in sex hormones in the body, and enhancing the affinity of tumor cells for growth factors.

4.2.1. Bladder Cancer

A meta-analysis discussed the relationship between various types of cancer and dietary GI and GL. Patients with

hyperglycemia and hyperinsulinemia are more likely to develop bladder cancer. Urinary tract infection is also one of the important causes of bladder cancer, and high-glycemic foods may increase the incidence of urinary tract infection [22]. In vitro studies have found that insulin can not only control blood sugar, but also promote the growth of epidermal growth factor and protease, and induce the proliferation of bladder cancer cells [39]. In addition, abnormal secretion of male hormones caused by blood sugar changes is also a potential factor in inducing bladder cancer [40].

4.2.2. Breast Cancer

Breast cancer is a malignant tumor caused by abnormal proliferation of breast cells. It has a very high incidence and high mortality rate in women. Diabetes complicated with breast cancer is also very common, and glucose has a nourishing effect on cancer cells. Breast cancer patients who do not control blood sugar for a long time and consume foods that increase blood sugar quickly are at risk of poor prognosis and high mortality [41]. The cause of breast cancer is still unclear, and age, menopause, eating habits, etc., can affect its occurrence. Women's hormone levels before and after menopause may also be a potential factor in inducing breast cancer. After menopause, women's estrogen secretion decreases, leading to problems with glucose absorption and transport in the body [42]. Insulin has the function of regulating hormones in the liver, increasing the synthesis of IGF-1 and sex hormone bioavailability. In addition, high GI foods are related to the synthesis of serum fat, C-reactive protein and other inflammatory biomarkers [43].

4.3. Lung Cancer

Lung cancer is one of the most common malignant tumors, and cigarettes are an important cause. Chun-Pin Chang et al. found that dietary GI and dietary GL are closely related to lung cancer [44]. Intake of high GI foods may accelerate the proliferation of cancer cells, and also cause blood sugar to rise and stimulate insulin secretion, prompting IGF growth factor to indirectly or directly affect the occurrence of lung cancer. In addition, patients with squamous cell lung cancer may also have a certain relationship with smoking and eating habits. Gastrointestinal absorption is associated with squamous cell carcinoma, and changes in insulin growth factor (IGF-1) levels can promote tumor cell mitosis. The IGF-1R receptor of squamous cell carcinoma behaves abnormally in smokers, thereby inducing the occurrence of lung cancer [45].

In summary, the intake of insulin, sex hormones and carbohydrates (CHO) are all related to blood sugar levels. The increase in the bioavailability of IGF growth factor promotes hormone secretion, thereby inducing the proliferation and migration of cancer cells.

5. Overview of Low GI Diet and Cancer

The "low GI" diet concept is a new diet that has become popular in recent years. At present, countries such as Australia and New Zealand are constantly improving the relevant regulations on GI marking, and China also issued relevant regulations on the GI marking of pre-packaged foods in 2019. The low GI diet pattern can lower blood sugar, promote fat consumption, and reduce intestinal absorption. It is an important means to prevent and treat diabetes and chronic diseases. In China, the dietary structure of residents is mainly cereals, among which carbohydrates account for a large

proportion, accounting for about 55%-65% of the total energy per day. It can be seen that cereal foods are closely related to human health. The carbohydrate content in food has a direct impact on postprandial blood sugar and the GI value of food. The GI value of food is also closely related to the processing and cooking method. The preparation of refined carbohydrates that is easy to digest and absorb will result in a higher GI value of food and poor blood sugar control. Some breads containing whole wheat flour have a low GI value because they are difficult to digest. Food components such as dietary fiber, protein, and fat can reduce the GI value of food, especially soluble dietary fiber has a significant effect on reducing the GI value of diet.

Studies have shown that consuming low-GI foods can produce a strong sense of fullness, which helps control food intake and thus reduce the absorption of glucose in the small intestine [46]. In China, there are many studies on the use of low-GI diets to intervene in type 2 diabetes and they have therapeutic value. Despite this, the development of low-GI diets in the prevention and treatment of tumors is still very slow. Cancer patients are affected by multiple factors such as blood sugar metabolism and hormones. Whether relying solely on a low-GI diet can control blood sugar and prevent decreased insulin sensitivity requires further experimental proof. Therefore, the clinical application value of applying and developing low-GI foods to prevent cancer is also a severe test currently faced.

6. Conclusion and Outlook

As people's awareness of self-health management gradually increases, major diseases that threaten people's quality of life, such as diabetes and cancer, are also receiving more and more attention. Nutritional support therapy is also regarded as an effective intervention method for the prevention and treatment of cancer. A low GI diet has been proven to be effective in controlling blood sugar and managing chronic diseases. Long-term maintenance of high blood sugar levels is not only one of the risk factors for the development of diabetes, but also one of the factors that induce cancer [47]. Sustained high blood sugar levels may lead to reduced insulin sensitivity and the occurrence of hyperinsulinemia, which will further lead to increased IGF-1 levels, thereby promoting cell mitosis. Insulin not only affects blood sugar levels, but also promotes cell division and has a certain connection with hormone metabolism-related cancers [48]. In addition, the diet of cancer patients is also very important. Long-term consumption of foods that increase blood sugar levels quickly may also promote cancer deterioration and poor prognosis.

This article describes the relationship between glycemic index (GI) and cancer, and the factors affecting blood sugar control in cancer patients with a low GI diet. On this basis, the relationship between changes in insulin and sex hormone levels and different cancers is explored. Based on previous studies, low GI dietary patterns have important clinical application value in the management of blood sugar control in diabetic patients. Although a number of clinical controlled studies have proven the benefits of a low GI diet, a high GI diet may affect insulin resistance and hormone levels, thereby indirectly affecting the occurrence of cancer. However, there are many causes that affect the onset of cancer, such as inflammatory response, metabolic abnormalities, and genetics, and it is still not possible to definitively prove the benefits of a low glycemic index diet for cancer.

In the future, in studies related to nutritional support and cancer, we hope to explore in depth the relationship between glycemic index (GI) and cancer prevention and treatment. Whether the development of low GI foods can help prevent the occurrence of cancer, it is also necessary to consider the detection method of GI values, the selection of raw materials during product development, and other factors that affect cancer.

In summary, there are many factors that affect the glycemic index and cancer. When studying the influencing factors between dietary GI and cancer, a large amount of clinical experimental verification is still needed.

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