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Relationship between Diabetes, Pancreatic Cancer and Diet

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Abstract

The pancreas is responsible for the regulation of blood sugar and the secretion of digestive enzymes. It performs these functions through its parts called exocrine and endocrine pancreas. Pancreatic cancer is suggestive of advanced age-onset diabetes when accompanied by typical symptoms such as unexplained weight loss, persistent abdominal or back pain, dyspepsia, vomiting, or steatorrhoea. Pancreatic cancer is one of the most aggressive diseases; it has a poor prognosis and despite efforts the five-year survival rate remains below 9%. Pancreatic cancer can arise in endocrine or exocrine cells. Pancreatic ductal adenocarcinoma is a type of exocrine pancreatic cancer that occurs in the head of the pancreas and smoking, increasing age, family history of pancreatic cancer, chronic pancreatitis, obesity and diabetes are risk factors for pancreatic ductal adenocarcinoma. There is bidirectional causality between diabetes and pancreatic ductal adenocarcinoma. Anti-diabetic drugs can also affect the development, progression, and outcome of pancreatic cancer, as they can directly affect the factors that influence the relationship between diabetes and pancreatic ductal adenocarcinoma. Insulin was associated with an increased risk of pancreatic cancer, while the use of metformin was found to be inversely related. For this reason, raising awareness of individuals and health personnel about a healthy lifestyle, including nutrition, and gaining the habit of practicing and maintaining it can contribute to the prevention of diabetes and pancreatic cancer.

Introduction

The pancreas is a gland that plays a vital role in the human body system. It consists of the head, neck, body and tail of the pancreas. This gland is divided morphologically into the endocrine and exocrine pancreas. The exocrine pancreas is responsible for the secretion of digestive juices, while the endocrine pancreas is effective in releasing hormones responsible for regulating blood sugar. Secretory cells called the islets of Langerhans perform the function of endocrine secretion. The insulin they secrete plays the most important role in the metabolism of glucose and insufficient or ineffective insulin secretion causes diabetes [1].

There are four subgroups of diabetes, according to the American Diabetes Association (ADA). It is termed Type 1 Diabetes (T1DM), an immune-mediated condition associated with beta cell destruction that often leads to absolute insulin deficiency. T2DM is known as a spectrum that includes varying degrees of peripheral insulin resistance and beta cell dysfunction. Type 1 diabetes is mostly seen in childhood and adolescence, while Type 2 diabetes usually occurs in people over 40 years of age. Type 2 diabetes is a condition in which blood sugar rises due to the pancreas' inability to secrete enough insulin or insufficient use of the secreted insulin. Type 4 DM refers to gestational or pregnancy-associated diabetes. T3cDM, which is among Type 3 DM categorized as 'other specific types of diabetes' by the ADA, is used to define DM, especially DM resulting from exocrine pancreatic diseases [2]. T3cDM is also called pancreatogenic or pancreatic DM.

There is bidirectional causality between diabetes and Pancreatic Ductal Adenocarcinoma (PDAC). Long-standing T2DM is a risk factor for the development of PDAC and PDAC is an assumed cause of diabetes [3]. Higher levels of circulating insulin and increased pressure on the pancreas to produce insulin are among the causes that lead to a possible risk of pancreatic cancer. At the same time, pancreatic cancer can lead to insulin resistance by increasing the amount of insulin produced by the pancreas, and pancreatic cancer can lead to a loss in insulin production capacity. Both conditions can trigger an increased risk of diabetes [4,5]. Identifying clinical features and biomarkers to differentiate cancer-associated type 2 diabetes may allow earlier detection of pancreatic cancer and thus improve management and survival.

Pancreatogenic Diabetes (T3cDM)

Type 3c diabetes (T3cDM), also known as pancreatogenic diabetes, refers to diabetes that results from pancreatic disease, including pancreatitis, cystic fibrosis, and pancreatic cancer. It is difficult to diagnose and difficult to manage because of the erratic fluctuations from hypoglycemia to hyperglycemia caused by metabolic abnormalities due to pancreatic tissue damage [6].

This type of diabetes generally occurs with pancreatic inflammation, pancreatic tumors or damage to the pancreas during surgical interventions. Any attack of acute pancreatitis can cause a temporary diabetic state and facilitate the development of diabetes later [7,8]. One study found no causal effect of long-standing diabetes on Pancreatic Cancer (PC), but findings suggest that PC causes new-onset diabetes [9]. The interaction between obesity, PC and T2DM has been reported to be complex.

Type 2 DM can cause pancreatic cancer or occur as a result of pancreatic cancer, while T3cDM occurs as a result of pancreatic damage [10]. Pancreatogenic diabetes can be seen in 5-10% of diabetes cases, while more than 85% of these cases are associated with chronic pancreatitis. Despite its metabolic properties and clinical course, T3cDM is not widely recognized by physicians. Diagnosis is often missed and patients are often misclassified. Failure to accurately diagnose pancreatogenic diabetes leads to inadequate medical treatment of these patients [11].

Due to the paucity of studies specifically investigating the treatment of T3cDM, current guidelines on disease management have been drawn from best practices applicable to T1DM and T2DM. Basically, although the goals of management are patient-specific management with individualized treatment goals, it is recommended to reduce fasting blood glucose and HbA1c to the safe range based on the patient's condition (such as age, comorbidities, and life expectancy). Cui and Andersen [12] suggested improving lifestyle factors for all patients, particularly obese individuals, suggesting concerted effort to lose weight, daily exercise, a diet restricted from refined carbohydrates, abstinence from alcohol, and quitting smoking.

Pancreatic Cancer

Pancreatic cancer ranks 14th among common cancer types in the world and 4th in cancer-related deaths [13,14]. Despite advances in the detection and management of pancreatic cancer, the 5-year survival rate is still only 9% [4]. Pancreatic cancer is caused by the uncontrolled proliferation of cells in the pancreas. It mostly occurs in the exocrine cells surrounding the pancreatic ducts and is called Pancreatic Ductal Adenocarcinoma (PDAC). PDAC is the most common form of pancreatic cancer with a sustained incidence of progression and is thought to represent the second cause of cancer-related deaths in Western countries by 2030 [15].

The risk of developing pancreatic cancer increases with age, and 90% of newly diagnosed patients are over the age of 55. The incidence of pancreatic cancer before the age of 30 years is low [16]. While the risk of pancreatic cancer was found to increase with high alcohol consumption (more than three drinks per day), no association was found with low and moderate alcohol consumption [17]. Smoking is a preventable risk factor for both diabetes and pancreatic cancer [18]. High consumption of saturated fat and red meat, but low intake of vegetables and folate are among the risk factors for pancreatic cancer [19]. Pancreatic cancer is suspected when advanced-onset diabetes is accompanied by typical symptoms such as unexplained weight loss, persistent abdominal or back pain, dyspepsia, vomiting, or steatorrhoea [20].

As various anti-diabetic drugs can directly affect key factors that mediate the relationship between T2DM and PDAC, some of these drugs may also have an impact on the development, progression and outcome of PDAC [21]. For example, Metformin is effective in preventing pancreatic and breast cancer [22]. But, individuals who take insulin therapy and have insulin resistance have a higher risk of developing pancreatic cancer. So, existing diabetes should be treated to reduce the risk of developing pancreatic cancer.

Furthermore, obesity is associated with an increased risk of cancer, including pancreatic cancer [23]. Obesity is a condition in which the body weight and fat ratio increase excessively when the energy taken in the diet is more than the energy spent. Foods and supplements in the diet to prevent obesity and diabetes will indirectly contribute to the prevention of pancreatic cancer.

PDAC and Diet

Epidemiological and experimental studies have shown a direct link between obesity, high Body Mass Index (BMI), weight gain, and an increased risk of developing pancreatic cancer. It is reasonable to assume that a high-calorie diet and/or high consumption of fats and sugars that predispose to overweight or obesity over time will have a negative impact on pancreatic cancer risk. In addition, high consumption of red meat has been found to increase the risk of several types of cancer, including pancreatic cancer [24]. On the other hand, there is also evidence that a healthy diet may play a role in protecting against pancreatic cancer. The 2020–2025 Dietary Guidelines (DGA) for Americans recommend consuming a diet rich in fruits, vegetables, and whole grains, along with a focus on maintaining a healthy weight by consuming the right amount of calorie and nutrient-dense foods [25].

It is known that pancreatic cancer and factors such as diabetes, chronic pancreatitis, obesity in its etiology are directly or indirectly related to the diet of individuals [26]. Dietary factors are up to 30% to 50% effective on pancreatic cancer, and there is evidence that some foods are at higher risk, while others are protective [23]. While a diet containing high fat, simple sugar and processed foods increases the risk of cancer; It has been reported that a diet with high antioxidant content (such as vegetables, fruits, and nuts) and a high fiber consumption, but low in saturated fat and sugar, have a reducing effect on the risk of pancreatic cancer development [24,27].

Macro Nutrients

A healthy lifestyle, regular exercise, non-smoking, and a low-fat and low-sugar diet can contribute to the prevention of pancreatic cancer. In a study investigating the effect of a high-fat diet on pancreatic cancer, a diet high in fat and calories accelerated the development of pancreatic intraepithelial neoplasia (PanIN) by causing obesity, metabolic disorders, and an inflammatory pancreatic environment in mice [28]. Diets with a high glycemic index and glycemic load increase insulin secretion in the body. With the increasing amount of insulin, the level of IGF in the body increases, and increased IGF can lead to an increase in the risk of cell transformation, changes in gene expression, and proliferation of tumor cells [29].

Consumption of red meat, processed meat (sausage, salami, sausage), fried foods, and other foods containing nitrosamines, which are a rich source of protein and cooked at high temperatures, may increase the risk of pancreatic cancer [4]. It is known that saturated fat intake with meat is also effective here. In a cohort study of red meat and high-temperature cooking on pancreatic cancer risk, low meat eaters (approximately 30% to 45% lower mortality) and vegetarians and vegans (approximately 50% lower mortality) were found to have low mortality to be diagnosed with pancreatic cancer compared to regular meat eaters [30]. The results of a meta-analysis showed that red meat intake increased the risk of pancreatic cancer by approximately 48%, while high intake of vegetables and fruits, especially citrus fruits and antioxidant-enriched vegetables and fruits, had a protective effect [31].

Phytochemicals and Dietary Fiber

It is well known that fruits, vegetables, whole grains, and nuts contain high amounts of phytochemicals, which are bioactive compounds classified as carotenoids, phenolics, alkaloids, nitrogen-containing compounds, and organosulfur compounds, which may protect against a variety of chronic diseases and cancer. Although the mechanism of action has not yet been fully elucidated, phytochemicals have been reported to have an anticancer effect [24]. Some of the mechanisms proposed to explain the anticancer properties of phytochemicals include antioxidant and anti-inflammatory effects; inhibition of cell proliferation, differentiation, adhesion and invasion; anti-bacterial and anti-viral effects and stimulation of immune functions; DNA damage repair; regulation of steroid hormone and estrogen metabolism; regulation of signal transmission pathways; enzyme regulation; inhibition of oncogene suppression and induction of tumor suppressor gene expression; cell differentiation and induction of apoptosis are counted [32].

Fruits and vegetables have a protective effect against pancreatic cancer and other cancers with the vitamins, minerals and antioxidants they contain. Antioxidants are compounds that are produced in the body or we get from the foods we eat, and can prevent cell damage. A diet full of red fruits such as red grapes, blueberries, strawberries, and raspberries rich in resveratrol (a powerful antioxidant), kaempferol, a flavonoid abundant in ginger, propolis, and teas, raw vegetables and fiber-rich whole grains can reduce the risk of pancreatic cancer [33,34].

In addition to the role of phytochemicals, dietary fiber, a major component of fruits, vegetables, whole grains and nuts, has been found to be inversely related to cancer risk. A case-control study of 326 pancreatic cancer patients in Italy found that soluble and insoluble fiber and fiber from fruit were inversely associated with pancreatic cancer, although no association was established between cereal fiber and pancreatic cancer risk [35]. On the contrary, in a study on the Mediterranean diet and cancer risk, it was determined that whole grains have a protective effect against various diseases against cancer types, including pancreatic cancer. In a prospective study conducted with female participants (n = 75,680), it was shown that 28 g of nuts consumed twice a week or more significantly reduced the risk of pancreas [36].

Not only food but also cooking methods are important in preventing cancer. Incorrect cooking methods can lead to loss of vitamins and minerals. Foods should not be over-purified so that fiber and antioxidant losses do not occur.

Calorie Restriction

In addition to a diet rich in fruits, vegetables, nuts, and whole grains, calorie restriction is another promising strategy that appears to be effective in protecting against cancer risk [23]. In fact, by regularly controlling the amount of calories consumed, a reduction in the level of insulin, insulin-like growth factor, leptin, adiponectin, plasminogen activator inhibitor, cytokines and vascular endothelial growth factor is achieved. These changes result in lower inflammation and growth factor signaling and reduced vascular disorders, reduced cancer risk and cancer progression [24]. These findings clearly demonstrate the link between a high-calorie diet and the likelihood of developing pancreatic cancer.

The Mediterranean diet, which is high in vegetables, fruits, fiber and unsaturated fatty acids, is a protective diet against cancer, obesity and diabetes [37,38]. Olive oil, nuts, whole grains, fruits and vegetables should be included in the daily diet; In addition, the consumption of fish and legumes 1 time to 2 times a week should be supported. Since the glycemic load will remain lower with such a diet, it may be protective against both the regulation of blood sugar in diabetes and the development of cancer in the long term. In the light of this information, it is an expected result that a healthy and functional diet individualized according to age, gender, activity level and other psychosocial characteristics will not only reduce the risks of diseases such as obesity, diabetes and cancer, but also positively affect the quality of life.

Conclusion

Gender, age, ethnicity, diabetes mellitus, family history of pancreatic cancer, genetic factors, chronic infections, non-O blood type, and chronic pancreatitis are among the non-modifiable risk factors for pancreatic cancer. In addition, lifestyle factors including excessive smoking and alcohol use, obesity, occupational exposures, nutrition and exercise are modifiable risk factors. A healthy lifestyle can protect against pancreatic cancer by preventing or delaying the development of obesity and diabetes, among many other health benefits.

In today's world, where the incidence of obesity, diabetes and many cancers is increasing as a result of negative changes in nutrition and lifestyle, raising awareness of individuals about healthy nutrition and gaining the habit of applying and maintaining healthy lifestyle components can be an important step in order to protect public health. For this purpose, interventions to increase awareness of health personnel, caregivers and health educators about the risk factors, early symptoms and prevention approaches of diabetes and pancreatic cancer are important in terms of reducing the frequency of the disease and providing early diagnosis and treatment opportunities.

Conflict of Interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. Informed consent was obtained for this publication.

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