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Obesity and pancreatic cancer: the underlying mechanisms

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Abstract

Obesity has emerged as a severe public health concern worldwide, with an increasing number of studies linking it to an increased risk of various forms of cancer, including pancreatic cancer. Although the underlying pathways behind this relationship are unknown, different putative biological and metabolic pathways have been discovered. These are examples of chronic low-grade inflammation, insulin resistance, altered hormone levels, and exposure to external environmental risk factors. These underlying processes are believed to combine with genetic and environmental variables in obese individuals to contribute to the development and progression of pancreatic cancer. More study is needed to thoroughly understand the complicated relationship between obesity and pancreatic cancer to create effective preventive and early detection measures for this fatal illness.

Introduction

Obesity is becoming more common among adults and children in the United States of America, as well as in many other nations. Obesity is a well-known risk factor for several illnesses, including pancreatic cancer. Obesity may cause an increase in pancreatic cancer incidence through a variety of methods. However, the precise causative pathway is unknown and may include various local and systemic changes caused by obesity. Understanding the chemicals and molecular signaling pathways that drive pancreatic cancer formation and growth is critical for creating tailored prevention/interception therapies (Eibl & Rozengurt, 2021).

Prevalence of obesity and pancreas cancer

Since 1975, the global number of obese people has nearly tripled. More than 1.9 billion individuals (39%) were overweight (body mass index (BMI) 25) in 2016, with over 650 million (13%) obese (BMI 30). In 2016, more than 340 million children and youth (ages 5-19) were overweight or obese, and 39 million kids under the age of five would be overweight or obese by 2022 (World Health Organization, 9 June 2021). In the United States of America, the latest data brief from the National Center for Health Statistics reports a prevalence of obesity in adults aged 20 years or older of 42.4% in 2017–2018, which is a considerable increase from 33.7% in 2007–2008 (Hales, Carroll, Fryar, & Ogden, 2020; Tzenios, Tazanios, & Chahine, 2022). There is no doubt that obesity is an enormous burden on the individual's health and society. Obesity itself has now been declared a chronic progressive disease and, in addition, a risk factor for multiple human diseases, including several types of cancer (Blüher, 2019).

Pancreatic cancer has an extremely poor prognosis and survival rate. The estimated 5-year survival rate ranges between 2 and 9% (Michaud & Cancer, 2016). The Global Cancer Observatory

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(GLOBOCAN) reports indicate a similar number of cases and deaths caused by pancreatic cancer in 2018, making it one of the most lethal malignancies in the world (Bray et al., 2018). It is the seventh leading cause of cancer death in males and females. The highest rates are reported in the US, Europe, and Australia, while the lowest are in Middle Africa and South–Central Asia. It is the 4th lethal cause of cancer death in America and the 6th in Europe (Ferlay et al., 2015). Some important risk factors majorly contribute to the pathophysiology of pancreatic cancer. These etiological factors include smoking, genetic factors, diabetes, obesity, alcoholism, and a sedentary lifestyle (Rawla, Thandra, & Sunkara, 2019).

Prevalence of obesity-linked pancreatic cancer

Obesity-related diseases have long been known to raise the incidence of various cancers, including pancreatic cancer. Obesity, as well as smoking, is one of the few controllable risk factors that enhance the probability of getting pancreatic cancer. This link has been widely demonstrated in many studies, including combined and meta-analyses (Chang & Eibl, 2019; Genkinger et al., 2011; Pang et al., 2017; Zhao, Liu, & treatment, 2020). A new study used Mendel randomized analysis on data from genome-wide association studies to assess the importance of various metabolic parameters on pancreatic cancer risk. Only BMI and fasting insulin levels were shown to be causally related to an elevated risk of pancreatic cancer in the study, not type 2 diabetes or dyslipidemia (Carreras-Torres et al., 2017). Parkin et al. conducted a survey in 2011 that determined that increased BMI was responsible for around 12% of all pancreatic malignancies (Parkin, Boyd, & Walker, 2011). Based on another cohort study, women with a BMI over 27.5 had a 20–37% increased chance of developing this disorder (Reeves et al., 2007). According to the American Cancer Society, men and women with a higher BMI are more susceptible to dying from pancreatic cancer. Additionally, obese patients typically experienced earlier disease onset and worse survival rates (Calle et al., 2002).

Obesity and pancreatic cancer: exploring the underlying mechanisms

Molecular mechanisms and signaling pathways contributing to clinical events that lead to pancreatic cancer are poorly understood. Still, it seems likely that multiple biological processes may be involved in the pathophysiology of pancreatic cancer (Cascetta et al., 2018). One explanation argues that the expansion of adipose tissue causes the accumulation of connective tissue, or desmoplasia, which promotes the survival and movement of malignant cells (Eibl et al., 2018). The desmoplasia comprises extracellular matrix proteins, pancreatic stellate cells, and immune cells. It is a metabolically active tissue that secretes an abundance of cytokines and growth factors and promotes cancer growth. Desmoplasia causes changes in overall tissue structure and accompanying interstitial fluid pressure, thereby contributing to chemoresistance. The role of desmoplasia in pancreatic cancer is still a matter of ongoing research (Blüher, 2019).

Another proposed mechanism underpinning the role of obesity on pancreatic cancer progression implicates the overproduction of circulating insulin by obese individuals. Hyperinsulinemia causes a rise in insulin growth factor (IGF)-1, which, after binding with its receptor, or the insulin-like growth factor receptor (IGFR), activates the mTOR, PI3K, and MAPK pathways. These well-

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known pathways in cancer biology promote cell proliferation and angiogenesis and inhibit apoptosis, thus fueling cancer growth. Many studies have repeatedly associated pancreatic cancer risk with markers of elevated glucose levels (Alemán et al., 2014).

Obese people frequently combine increased food intake with poor dietary practices, which enhances the consumer's exposure to carcinogens. Despite some inconsistencies in the published data, a meta-analysis of 11 studies found a link between processed meat intake, meat cooked at high temperatures (such as when fried or grilled), and preserved foods (Larsson & Wolk, 2012). Most processed meat products utilize nitrate additives, which have been strongly associated with both men's and women's risk of developing pancreatic cancer. N-nitroso compounds, another potent carcinogen, may also be present in processed beef (Coss, Cantor, Reif, Lynch, & Ward, 2004). An experimental animal model study shows that these compounds are risk factors for pancreatic cancer development (Risch, 2003).

Preventive measures for pancreatic cancer

Few studies evidence the impact of weight loss through physical activity on cancer development (Tzenios, Tazanios, Poh, & Chahine, 2022). Most research has linked the favorable effects of organized exercise to angiogenesis rather than weight reduction (Cormie et al., 2014). When training and nutrition fail to generate satisfactory results, bariatric surgery is used to aid long-term weight loss in very obese people. Even after a 20-year follow-up, forms of bariatric surgery resulted in significant weight reduction. Swedish research enrolled almost 4000 obese individuals, with 2010 undergoing bariatric surgery and 2036 serving as controls. After a 10-year follow-up, the bariatric surgery group had a 40% reduced incidence of obesity-related cancers than the control group (Puzziferri et al., 2014; Sjöström et al., 2009)

Conclusion

This article investigates the link between higher BMI and pancreatic cancer risk. According to the paper, obesity causes the production of many inflammatory factors, which contribute to the formation of cancer cells in the pancreas. The essay emphasizes the impact of hormones such as insulin in boosting cancer cell development. The article also examines the role of food and lifestyle variables, such as high-fat consumption, in developing pancreatic cancer. According to the study, lowering weight and living a healthy lifestyle can help minimize the chance of pancreatic cancer.

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