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Obesity and prostate cancer: the influence of metabolic syndromes

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Abstract

Obesity is a significant issue for public health that is linked to a variety of chronic ailments, including cancer. Prostate cancer is the most frequent disease in men, and there is growing evidence that obesity might impact prostate cancer risk and prognosis. This article reviews the present body of scientific knowledge on the link between obesity and prostate cancer, emphasizing the involvement of metabolic syndromes. It examines the evidence indicating a direct relationship between obesity and prostate cancer risk and the likely processes behind this link, such as alterations in hormonal, immune-modulatory, and metabolic pathways. Furthermore, it investigates the influence of metabolic disorders, including insulin resistance and metabolic syndrome.

Introduction

Overweight and obesity are defined by the World Health Organization (WHO) as excessive or abnormal accumulation of fat that leads to a public health concern. These problems have been linked to an increased risk of various chronic illnesses, including diabetes and cardiovascular disease. Furthermore, multiple studies have linked obesity to an increased risk of various malignancies. (Bandini, Gandaglia, & Briganti, 2017). It is worth noting that this disease may play a role in the pathophysiology of prostate cancer. Several preclinical trials have revealed that various metabolic and molecular processes are involved in the link between obesity and the incidence of prostate cancer (Parikesit, Mochtar, Umbas, & Hamid, 2016).

Prostate cancer is the most commonly diagnosed nonskin cancer and the second leading cause of cancer deaths in US men (Hsing & Devesa, 2001). Prostate cancer is the second most commonly diagnosed cancer and the sixth leading cause of cancer death among men worldwide (N. Tzenios, M. E. Tazanios, & M. Chahine, 2022), with an estimated 1 276 000 new cancer cases and 359 000 deaths in 2018. The worldwide prostate cancer burden is expected to grow to almost 2.3 million new cases and 740 000 deaths by 2040 simply due to the growth and aging of the population (Ferlay et al., 2018). Older age, black race, and a family history of the disease are the only well-established risk factors for prostate cancer. There is some evidence that body fatness, adult-attained height, dairy products, a diet high in calcium, and low plasma selenium and alpha-tocopherol concentrations increase the risk of prostate cancer (Baron, 1996; Hayes et al., 1999).

The biological mechanisms linking westernization to increased prostate cancer risk are unclear. However, it has been hypothesized that the increased prevalence of obesity and metabolic syndrome resulting from lifestyle changes associated with westernization, such as physical inactivity and a higher intake of dietary fat and meat, may explain part of the rising rates in Asian populations (Hsing, Sakoda, & Chua, 2007).

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Obesity or higher BMI-associated metabolic syndromes as an etiological agent for prostate cancer

Over the past two decades, the prevalence of metabolic syndrome has been increasing worldwide and has become a major public health problem in several countries. (Hsing, Sakoda, & Chua Jr, 2007). It is an emerging clinical problem of enormous proportions and is associated with the global epidemic of obesity and diabetes mellitus (N. Tzenios, M. Tazanios, & M. Chahine, 2022). Metabolic syndrome is a common clinical condition in countries with a high incidence of obesity and western dietary patterns. Its etiology is complex and comprises multiple factors, including excess weight, a sedentary lifestyle, high-energy intake, and unknown genetic factors (Laaksonen et al., 2002).

Metabolic syndrome is considered an emerging hypothesis in the etiology of prostate cancer. Several studies have found that metabolic syndrome features may predict prostate cancer risk (McGrowder, Jackson, & Crawford, 2012).

It is estimated that 12–37% of the Asian population and 12–26% of the European population suffer from metabolic syndrome (Ranasinghe, Mathangasinghe, Jayawardena, Hills, & Misra, 2017). Metabolic syndrome is a cluster of at least three out of five cardio-metabolic abnormalities that occur concomitantly. These abnormalities are abdominal obesity, hyperglycemia, hypertriglyceridemia, low HDL cholesterol, and hypertension (Sigit et al., 2020). Other components of metabolic syndrome include prothrombotic and proinflammatory states. Central obesity is often present, but the syndrome does occur in its absence. Lean individuals exhibit a wide range of insulin sensitivity and may have levels as low as those of obese insulin-resistant subjects (McGrowder et al., 2012).

Metabolic syndrome is thought to play a role in the etiology of prostate cancer. Several groups of investigators have suggested that features of the metabolic syndrome may be predictive of prostate cancer risk (McGrowder et al., 2012). The body of scientific data revealed that there is a positive relationship between metabolic syndrome and prostate cancer (Lund Håheim, Wisløff, Holme, & Nafstad, 2006), while some studies have reported an inverse relationship in a mixed population (Tande, Platz, & Folsom, 2006) and no relationship (Martin et al., 2009).

The link between metabolic syndromes and the progression of prostate cancer

Metabolic syndrome is an emerging hypothesis in the etiology of prostate cancer, although the evidence for this link is limited. Metabolic syndrome also called insulin resistance syndrome, is defined as a constellation of metabolic abnormalities, including glucose intolerance (fasting plasma concentrations > 110 mg/dL), dyslipidemia (serum triacylglycerol concentration ≥ 150 mg/dL, serum HDL concentration < 40 mg/dL), hypertension (blood pressure ≥ 130/85 mm Hg), and obesity (a waist circumference of >102 cm). A recent community-based case-control study of African Americans reported a 90% excess risk of prostate cancer associated with metabolic syndrome (Beebe-Dimmer, Dunn, Sarma, Montie, & Cooney, 2007).

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Some studies reported an inverse relationship between metabolic syndrome's components and prostate cancer's pathophysiology (Hsing, Sakoda, & Chua, 2007). While other studies (Laukkanen et al., 2004; Lund Håheim et al., 2006) reported a direct association between the metabolic syndrome's components and the progression of prostate cancer.

Metabolic syndrome and prostate cancer: Under the underlying mechanisms

Several mechanisms, including steroid (sex) hormones, insulin and IGF signaling, and inflammatory pathways, might explain the relationship between obesity, metabolic syndrome, and prostate cancer risk.

Association of hormonal component of metabolic syndrome with prostate cancer

The relationship between prostate cancer, sex hormones, and obesity is multifaceted, and the underlying biological processes are unclear. The prevailing orthodoxy about androgens and prostate cancer is that greater androgen concentrations elevate the prostate cancer risk. Intracellularly, testosterone is transformed into dihydrotestosterone (DHT), and DHT then interacts with the androgen receptor and its coactivators to generate an intracellular complex, which therefore links to the androgen response elements in the prostate gene to activate a cascade of androgen signaling (Hsing, Reichardt, & Stanczyk, 2002). Therefore, obesity may protect against prostate cancer as obese men have slightly lower blood testosterone levels, significantly lower levels of sex hormone-binding globulin, and greater estrogen levels (Gapstur et al., 2007). More recent data reveal that greater blood total testosterone concentrations are connected with a reduced risk of high-grade (Gleason 7) prostate cancer but an increased risk of low-grade tumors. At the same time, estradiol is associated with a lower risk of nonaggressive cancer but not an aggressive disease (Platz et al., 2005). These results demonstrated the intricate interlinkages between obesity and serum sex hormones and their varied influence on prostate cancer. They also support the variable effect of obesity on prostate cancer subtypes.

The insulin growth-like factor (IGF) signaling pathway.

The IGF pathway is one possible reason underlying the relationship between metabolic syndrome and prostate cancer. IGF-I is essential for cellular multiplication, differentiation, and apoptotic reduction. Obesity is linked to increased unbound or bioavailable IGF-I, and various epidemiologic studies have found a link between IGF-1 and prostate cancer risk (Kaaks, Lukanova, Sommersberg, & diseases, 2000; Nelson, De Marzo, DeWEESE, & Isaacs, 2004).

The inflammatory signaling pathways

Adipose tissue is now an active organ that secretes many proteins, including cytokines and hormone-like substances such as leptin and adiponectin (Sun et al., 2006). Obesity has been linked to low-grade chronic inflammation, with invading macrophages inside adipose tissue and elevated levels of inflammatory cytokines such as tumor necrosis factor-, interleukin-6, and C-reactive protein (Khanna, Khanna, Khanna, Kahar, & Patel, 2022). Chronic inflammation is one potential pathway between obesity and prostate cancer. A growing body of evidence supports the concept

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that chronic inflammation plays a role in prostate cancer development (Sfanos & De Marzo, 2012). Accumulating data support the hypothesis that chronic inflammation contributes to prostate carcinogenesis (Sun et al., 2006).

The association between higher BMI and prostate cancer is complicated and multifaceted. While obesity may not cause prostate cancer directly, it can raise the risk by increasing the development of metabolic disorders such as insulin resistance and inflammation. Furthermore, obesity may influence prostate cancer progression by changing the hormones and growth factors involved in the condition. Given these findings, people must maintain a healthy weight and lifestyle to lower their chance of acquiring prostate cancer and other related health problems.

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