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Research Progress on the Association between Obesity and Prostate Cancer

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Abstract

The complex association between obesity and prostate cancer necessitates exploring how obesity impacts the incidence, progression, treatment response, and prognosis of prostate cancer. An analysis was conducted to determine the potential adverse effects of obesity on prostate cancer treatment, including changes in drug metabolism and surgical complications. It also discusses how obesity increases the risk of disease progression and recurrence. Further emphasis was provided to the importance of comprehensive interventions to reduce the risk of prostate cancer through lifestyle modifications (including healthy diet, moderate exercise, and maintaining normal weight), pharmacological treatments (such as potential drugs targeting obesity and prostate cancer-related mechanisms), and regular check-ups and screenings. Lastly, the work envisions future research directions, including exploring the specific mechanisms linking obesity and prostate cancer, designing more scientific clinical trials, and enhancing interdisciplinary cooperation. These opportunities and challenges aim to provide references and insights for future research and development.

Key words obesity, prostate cancer, treatment response, prognosis, lifestyle modification, pharmacological treatment, clinical trials, interdisciplinary cooperation, gene-environment interaction, mechanism research

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Introduction

Prostate cancer is the most common malignancy of the genitourinary system among men [1-5]. Its incidence and mortality rates continue to dominate a significant position, posing a severe challenge to men's health worldwide [6, 7]. With the aging population and changes in lifestyle, the incidence of prostate cancer is increasing globally, especially in developed countries, where it has become one of the key factors affecting men's quality of life and life expectancy [8-10].

At the same time, the obesity problem is showing an alarming growth trend globally, becoming a public health crisis that cannot be ignored [11-14]. Obesity not only affects an individual's appearance and self-esteem but, more importantly, it is closely related to the development of various chronic diseases, including but not limited to cardiovascular diseases, type 2 diabetes, hypertension, and certain types of cancer [15, 16]. In an obese state, the abnormal accumulation of adipose tissue leads to energy metabolism disorders, chronic low-grade inflammation, insulin resistance, and hormone imbalances [17-20]. These complex physiological and pathological changes collectively increase the risk of various diseases.

Against this backdrop, the complex association between obesity and prostate cancer has gradually attracted widespread attention from researchers [21-24]. Multiple epidemiological studies have shown a significant correlation between obesity and the risk of prostate cancer, disease progression, and prognostication [25-28]. Although the specific mechanisms of this association are not yet fully elucidated, it is attracted significant attention. Understanding the intrinsic links between obesity and prostate cancer not only helps us better understand the pathogenesis of prostate cancer but also provides new ideas and strategies for its prevention, early diagnosis, and personalized treatment [29-31].

Therefore, this review highlights the latest research progress on the association between obesity and prostate cancer. By reviewing relevant literature (provide key words of the study and database surfed), a systematic analysis was performed for potential mechanisms by which obesity affects the occurrence and development of prostate cancer. In this regard, the review provides valuable references for researchers in related fields and raise public awareness of the issue of the association between obesity and prostate cancer. This, in turn, will promote the adoption and dissemination of healthy lifestyles, effectively reducing the incidence and mortality rates of prostate cancer.

Epidemiological association between obesity and prostate cancer

In the global public health landscape, the epidemiological association between prostate cancer and obesity has become increasingly prominent, emerging as a significant topic of medical research. With the continuous accumulation and analysis of medical data, an undeniable phenomenon has gradually emerged: the incidence rates of prostate cancer and obesity are rising synchronously worldwide [32, 33]. This trend transcends geographical boundaries, observable in both developed and developing countries, suggesting a potentially universal association between the two.

Firstly, on a global scale, the incidence of prostate cancer has significantly increased over the past few decades. This trend aligns almost synchronously with the global prevalence of obesity. Obesity, regarded as a "pandemic" of modern society, seems to share a subtle connection with the increasing incidence of prostate cancer [34]. Although it cannot yet be conclusively stated that obesity directly causes prostate cancer, the correlation between the two is undeniable [35, 36]. Further analysis of research results from various geographical regions reveals some inconsistencies regarding the association between obesity and prostate cancer [37, 38]. In developed countries including Europe and North America, where related research began earlier and comprises of comprehensive medical data systems, the research results are relatively rich and in-depth. Some large-scale epidemiological studies indicate that obese men have a significantly higher risk of developing prostate cancer compared to non-obese men [39, 40]. This association is particularly evident in high-grade or advanced prostate cancer. However, in Asian countries such as China, where the incidence of prostate cancer is also on the rise in recent years, studies on the association between obesity and prostate cancer are relatively scarce, and their conclusions are inconsistent [40, 41]. This inconsistency may be related to differences in genetic background, lifestyle, dietary habits, and medical standards across regions. Exploring the association between obesity and prostate cancer, an issue that cannot be ignored is the standardization of obesity definitions. Currently, Body Mass Index (BMI) is widely used as a common indicator for assessing obesity [43]. BMI, is calculated by dividing a person's weight in kilograms by the square of their height in meters, provides a straightforward reflection of an individual's weight status. However, it is important to note that BMI is not a perfect assessment standard, as it does not distinguish between fat and muscle mass, nor does it indicate the distribution of fat within the body. Therefore, relying solely on BMI to evaluate the association between obesity and prostate cancer may have certain limitations. Additionally, the applicability of BMI standards varies among different populations. For instance, Asian populations may have higher body fat percentages and lower muscle mass at the same BMI, suggesting that lower BMI thresholds might be needed to define obesity in these groups [41]. Lastly, it is crucial to emphasize that obesity is not the sole risk factor for prostate cancer. The occurrence of prostate cancer is a complex process involving multiple factors and steps, including interactions among genetic, environmental, and lifestyle factors. Age, family history, dietary habits, and sex hormone levels may all influence the incidence of prostate cancer [44]. Therefore, when discussing the association between obesity and prostate cancer, these factors should be comprehensively considered to avoid viewing obesity as the only or decisive factor. Future research should also explore the interactions between obesity and other risk factors to more comprehensively uncover the pathogenesis of prostate cancer.

Potential mechanisms by which obesity influences the occurrence and development of prostate cancer

In delving into the complex relationship between obesity and prostate cancer, the focus remains on a series of potential biological mechanisms that reveal how obesity affects the occurrence and development of prostate cancer (**Figure 1**).

Firstly, changes in hormone levels, particularly the imbalance of androgens and insulin-like growth factor (IGF), serve as key links between obesity and the increased risk of prostate cancer [45, 46]. Androgens, as vital hormones in the male body, play a crucial role in the normal growth and development of the prostate [47]. However, when androgen levels are abnormally elevated, they may act as "catalysts" for prostate cancer. In an obese state, adipose tissue is not only an energy reservoir but also an active endocrine organ that secretes various hormones and cytokines, some of which can influence androgen metabolism and function [48]. For example, aromatase in fat cells can convert androgen precursors into estrogens, leading to a relative increase in estrogen levels [47]. Estrogen has been shown to promote the proliferation of prostate cancer cells. Additionally, obesity may indirectly increase the bioavailability of free androgens by affecting the synthesis

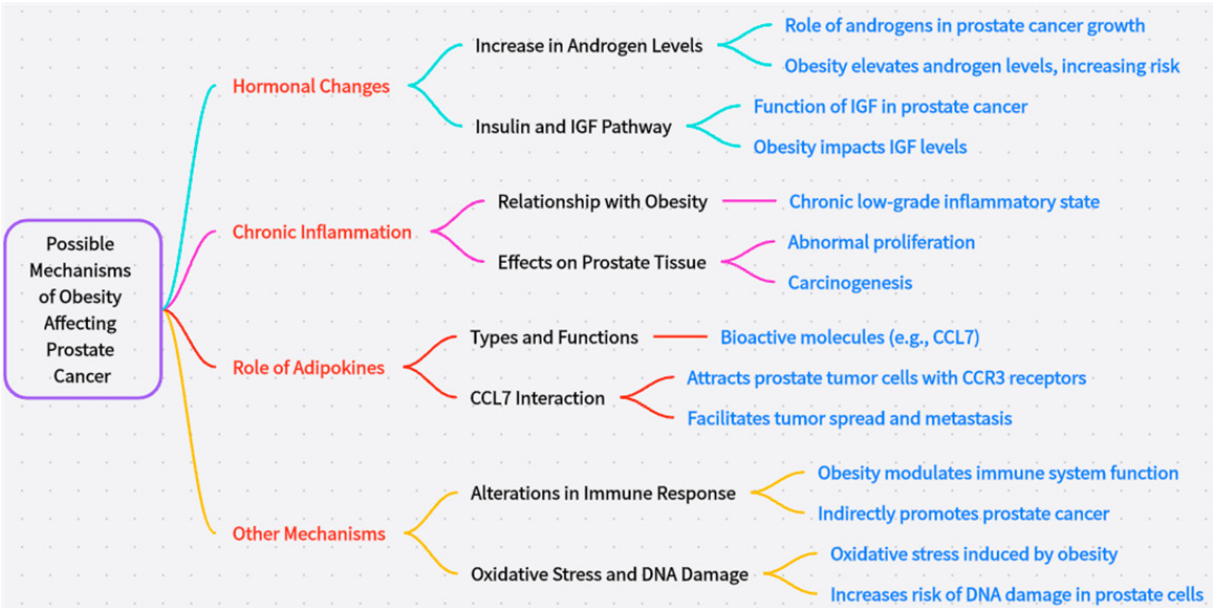

Figure 1. Possible mechanisms of obesity affecting prostate cancer.

and secretion of sex hormone-binding globulin (SHBG), thereby further increasing the risk of prostate cancer [48].

Simultaneously, the insulin and insulin-like growth factor (IGF) pathways also play significant roles in the occurrence and development of prostate cancer [49]. Obesity is often associated with insulin resistance and hyperinsulinemia, a condition in which the pancreas secretes more insulin to maintain blood glucose levels. High levels of insulin not only regulate glucose metabolism but also may promote the proliferation and survival of prostate cells by activating pathways such as the IGF-1 receptor (IGF-1R). IGF-1 is a powerful growth factor closely related to the growth, differentiation, and invasiveness of prostate cancer cells. In an obese state, increased secretion of IGF-1 by fat cells, along with enhanced IGF-1 bioactivity due to insulin resistance, acts on prostate tissue and increases the risk of prostate cancer.

Beyond hormonal changes, chronic inflammation is another important factor by which obesity promotes prostate cancer. Chronic low-grade inflammation caused by obesity is an adaptive response to excess fat accumulation. In an obese state, immune cells such as macrophages and T cells in adipose tissue are activated and release a large number of inflammatory factors and chemokines, such as tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), and chemokine CCL7 [50]. These inflammatory mediators not only regulate systemic inflammatory responses but also directly act on prostate tissue, promoting abnormal proliferation and carcinogenesis. CCL7, in particular, is a chemokine secreted by fat cells that can specifically attract prostate tumor cells expressing the CCR3 receptor, creating a microenvironment conducive to tumor growth and metastasis.
Moreover, various bioactive molecules secreted by fat cells influence the occurrence and development of prostate cancer through other pathways. Adipokines such as leptin, adiponectin, and resistin play crucial roles in regulating energy metabolism, immune responses, and cell proliferation [51]. Leptin, for example, is considered a potential pro-carcinogenic factor that can promote the proliferation and invasion of prostate tumor cells by activating multiple signaling pathways [52]. In contrast, adiponectin has anti-tumor effects, and its levels decrease in obesity, potentially weakening the body's defense against prostate cancer [53].

Finally, obesity may indirectly promote the occurrence and development of prostate cancer by affecting immune responses and increasing oxidative stress. In an obese state, the immune system may undergo functional changes, such as reduced immune cell numbers and decreased functionality, which can impair the body's ability to surveil and eliminate prostate cancer cells. Additionally, obesity is accompanied by increased oxidative stress, with excessive free radicals and oxidative products potentially damaging prostate cell DNA, increasing the risk of genetic mutations and carcinogenesis. These mechanisms collectively make obesity a significant risk factor for the occurrence and development of prostate cancer.

The impact of obesity on prostate cancer treatment and prognosis

In the field of prostate cancer treatment, obesity is not only a potential risk factor but also a condition that can profoundly impact treatment outcomes and patient prognosis [54, 55]. Obese patients undergoing treatment for prostate cancer often face a variety of complex challenges. These challenges are not only evident in the adverse reactions during treatment but also directly relate to disease progression, recurrence, and patient survival rates.

Firstly, obese patients may experience various weight-related adverse reactions during prostate cancer treatment. Drug therapy, a crucial component of comprehensive prostate cancer treatment, often sees its efficacy influenced by the patient's weight and drug metabolism capacity. Due to the higher fat content in obese patients, drug distribution and metabolism in the body can change, affecting the bioavailability and therapeutic effect of medications. For example, certain chemotherapeutic drugs may have a reduced clearance rate in obese patients, leading to higher drug concentrations and an increased risk of toxic side effects. Additionally, obesity can affect the response to hormone therapy, as hormonal imbalances in obese individuals may interfere with the effectiveness of such treatments.

Surgical treatment is another key modality for prostate cancer, but obese patients face higher risks during surgery [56, 57]. Increased abdominal fat in obese patients complicates the surgical

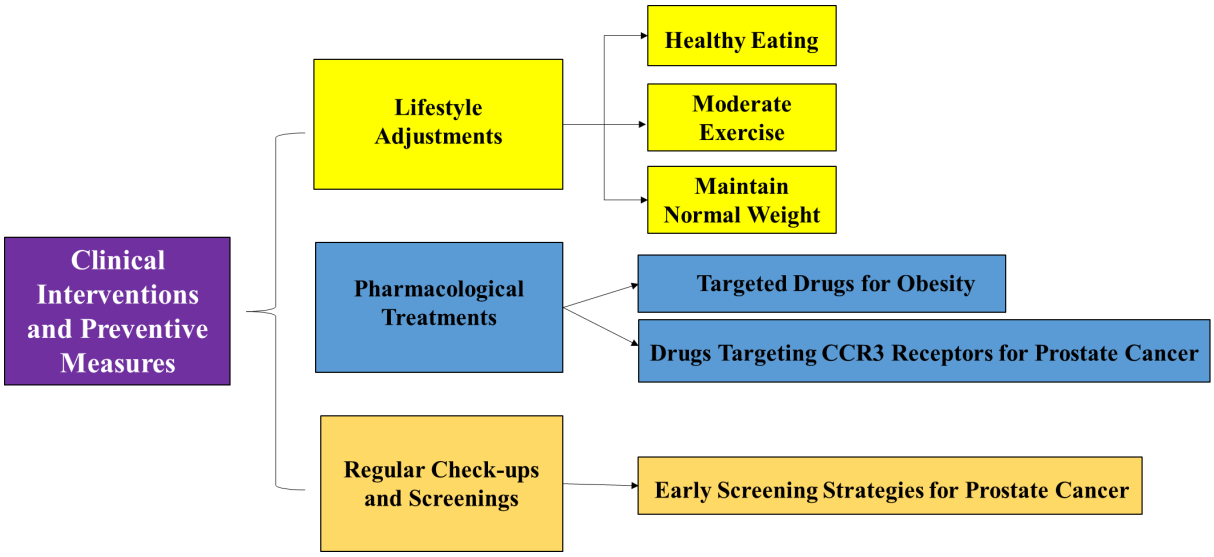

Figure 2. Clinical interventions and preventive measures.

field, making the procedure more challenging and increasing the difficulty of surgical maneuvers. This not only prolongs the surgery time but also raises the incidence of surgical complications such as bleeding, infection, and wound healing. Moreover, obesity can affect patients' responses to anesthesia, heightening the risk of postoperative respiratory and cardiovascular complications.

Beyond adverse reactions during treatment, obesity significantly increases the risk of disease progression and recurrence in prostate cancer patients. The persistent presence of chronic inflammation and abnormal secretion of adipokines in obese individuals create a favorable environment for the growth and spread of prostate cancer cells. These inflammatory factors and adipokines not only promote the proliferation and invasiveness of prostate cancer cells but also may alter the immune status of the tumor microenvironment, making it easier for tumor cells to evade immune surveillance and elimination. Consequently, obese patients often have higher recurrence rates and faster disease progression after treatment compared to non-obese patients.

Ultimately, obesity also significantly affects the overall mortality and prostate cancer-specific mortality rates in these patients. Numerous studies have shown that obesity is a critical predictor of poor prognosis in prostate cancer patients [58]. Due to the combined effects of metabolic disorders, reduced immune function, and lower treatment tolerance, obese patients have significantly higher all-cause and prostate cancer-specific mortality rates than non-obese patients. This not only increases the risk of patient death but also adds to the burden on healthcare resources and socioeconomic costs.

In summary, obesity plays a crucial role in the treatment and prognosis of prostate cancer. To improve treatment outcomes and prognosis for obese prostate cancer patients, a multifaceted approach is necessary. This includes optimizing treatment plans, enhancing perioperative management, controlling body weight, and promoting healthier lifestyles. Additionally, further research into the mechanisms linking obesity and prostate cancer is needed to provide a scientific basis for developing more precise and effective treatment strategies.

Clinical interventions and preventive measures

When addressing the impact of obesity on prostate cancer, the implementation of clinical interventions and preventive measures becomes crucial. These measures not only focus on individual behavioral changes but also involve potential applications of pharmacological treatments and the importance of regular check-ups and screenings, forming a comprehensive protective network [59].

Firstly, lifestyle modifications are fundamental and critical in preventing prostate cancer, particularly for obese patients [60, 61]. This requires individuals to fundamentally change unhealthy habits and adopt a healthier lifestyle. Maintaining a balanced diet means reducing the intake of high-fat, high-calorie foods and increasing the proportion of vegetables, fruits, whole grains, and high-quality protein-rich foods to ensure adequate nutrition without overburdening the body. Additionally, regular physical activity is indispensable. It promotes metabolism, enhances cardiovascular function, and helps maintain a healthy weight. For those who are already overweight or obese, gradual weight loss through a reasonable diet and regular exercise can positively impact reducing the risk of prostate cancer.

Besides lifestyle changes, pharmacological treatments offer new possibilities for intervening in mechanisms related to obesity and prostate cancer [62, 63]. With advances in medical research, scientists are gradually uncovering the complex interactions between obesity and prostate cancer, leading to the development of various potential therapeutic drugs. For example, targeted drugs against the chemokine receptor CCR3 have shown promising prospects in prostate cancer treatment. These drugs specifically block the binding of the CCR3 receptor to its ligands, interfering with the migration and invasion processes of prostate cancer cells and thus inhibiting tumor progression. Although these drugs are currently in clinical trials, their unique mechanisms and preliminary efficacy data have garnered widespread attention. As research progresses and technology advances, these drugs are expected to offer more personalized and precise treatment options for prostate cancer patients.

Lastly, regular check-ups and screenings are invaluable for the early detection of prostate cancer, significantly improving treatment outcomes and survival rates [65, 66]. This is particularly important for high-risk groups, such as obese individuals. Regular

prostate cancer screenings, including serum prostate-specific antigen (PSA) testing and digital rectal exams, can detect potential prostate cancer lesions early, allowing timely intervention. Additionally, for patients already diagnosed with prostate cancer, regular follow-ups and check-ups are essential. They enable doctors to monitor disease progression and treatment response, adjusting treatment plans to achieve optimal results.

In summary, clinical interventions and preventive measures play a vital role in mitigating the impact of obesity on prostate cancer. Through proactive lifestyle adjustments, rational use of pharmacological treatments, and strengthened regular check-ups and screenings, we can effectively reduce the risk of prostate cancer, improve treatment outcomes, and enhance the quality of life for patients (**Figure 2**).

Summary and outlook

In exploring the complex relationship between obesity and prostate cancer, faces numerous challenges and opportunities. Firstly, in-depth mechanistic research is essential. Although many studies have revealed potential links between obesity and prostate cancer, the specific molecular mechanisms, gene-environment interactions, and how these mechanisms collectively influence the development of prostate cancer require further investigation. This necessitates more detailed research at the genetic, protein, and metabolic pathway levels to fully understand how obesity alters the biological characteristics of prostate cancer and to provide a scientific basis for developing more effective intervention strategies.

Furthermore, the design of clinical trials is a crucial direction for future research. To more accurately assess the impact of obesity on prostate cancer and the efficacy of various interventions, there is need to design more scientific and comprehensive clinical trials. These trials should fully consider individual patient differences, the diversity of treatment regimens, and the necessity of long-term follow-up to ensure the reliability and reproducibility of results. Additionally, with the advent of the precision medicine era, one should explore clinical trial designs based on personalized information such as patient genotype and metabolic state to provide more precise treatment recommendations.

Interdisciplinary collaboration plays a vital role in addressing the association between obesity and prostate cancer. Close cooperation among disciplines such as endocrinology, oncology, and nutrition will provide broader perspectives and richer resources, promoting rapid development in this field. By combining research findings and technological methods from various disciplines, we can gain a deeper understanding of the interaction mechanisms between obesity and prostate cancer. This approach can lead to the development of more effective prevention and treatment strategies. This interdisciplinary collaboration not only enhances the breadth and depth of research but also facilitates the translation and application of research outcomes, contributing to patient health and well-being.

In conclusion, the complex association between obesity and prostate cancer and its potential mechanisms still require continuous exploration and in-depth research. Through the implementation of comprehensive intervention measures, including healthy lifestyle adjustments, appropriate pharmacological treatments, and regular check-ups and screenings, can effectively reduce the risk of prostate cancer and improve patient prognosis. Looking to the future, the call for more interdisciplinary cooperation and communication to jointly advance the development of this field and contribute wisdom and strength to overcoming this challenge.

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Ethical policy

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study. Approval from institutional ethical committee was taken.

Availability of data and materials

All data generated or analysed during this study are included in this publication.

Author contributions

Hang Xu, Yingshuang Tang searched academic literature and wrote the draft manuscript; Xiaorui Zhang and Xian Zhang did the data analysis and language editing; Along Kang supervised the review writting progress and approved the final manuscript submission.

Competing interests

Authors report no conflict of interest.

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