HEALTH IS INDEED A MAN'S THING: A REFLECTIVE ANALYSIS OF PROSTATE CANCER

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ABSTRACT

Prostate cancer is a malignant disease resulting from the disordered growth of cells, with morphological, structural and metabolic alterations, as well as accelerated division and genetic mutations. This neoplasm can invade adjacent organs and, in more severe cases, can reach places far from its origin. It is a disease that is usually associated with several triggering factors, a situation that proves its epidemiological importance in the country. It is a comprehensive review of the literature based on the narrative synthesis of scientific evidence. In clinical practice, it is observed that, in most cases, men only seek care when the disease is already installed, with greater chances of complications and early deaths. Because of this, it is of fundamental importance to include the male population in the health-disease process, so that the strong social and cultural influence rooted over the years and generations can give way to protagonism in health.

Keywords: Health promotion. Men's health. Prostate neoplasms.

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INTRODUCTION

Prostate cancer is recognized as a neoplasm of the elderly, since about three-quarters of cases in the world occur after the age of 65. In Brazil, the high incidence rates can be partially justified by the improvement of diagnostic methods, quality of information systems, as well as the increase in life expectancy (Brasil, 2020).

In this sense, in Brazil, the most incident types of cancer (except non-melanoma skin) are prostate (29.2%), colon and rectum (9.1%), lung (7.9%), stomach (5.9%) and oral cavity (5.0%). It is estimated that 65,840 cases of prostate cancer are diagnosed in the country annually. It is the sixth cause of mortality in the world, and in 2030, there are projections of approximately five hundred thousand deaths, with more deaths in underdeveloped countries (Peloso-Carvalho et al., 2021).

The etiology of prostate cancer is not yet fully known. However, evidence suggests that its origin involves a complex interaction between genetic and environmental causes. Therefore, the main risk factors are age (more than 3/4 of cases affect men over 65 years old); black ethnicity; exposure to ultraviolet radiation; Smoker; alcoholic; family history; mutations such as BRCA 1 and 2, HPC-1; and unhealthy diet - high-fat diet and smoked red meat (Iser et al., 2022).

There is also occupational exposure to chemical agents, which is responsible for 1% of cases (Brasil, 2021). In addition, it has been suggested that a history of sexually transmitted infections and/or prostatitis, as well as vasectomy, would be risk factors for prostate cancer. However, such associations proved to be inconsistent in later studies (Oliveira et al., 2021).

Among the conditions that can most favor the prevention of prostate cancer, a healthy diet stands out, especially with a diet rich in fruits, vegetables, legumes, whole grains and cereals and with less fat, especially those of animal origin; maintenance of body weight according to height; practice of physical activity at least thirty minutes a day and five times a week; and smoking cessation and alcoholism (Who, 2020).

Thus, considering that this disease represents a significant challenge for health systems worldwide due to its high incidence and impact on morbidity and mortality, it is justified to carry out this study for a better investigation. Therefore, the objective was to analyze the main available evidence on prostate cancer.

METHOD

It is a comprehensive review of the literature based on the narrative synthesis of scientific evidence. To this end, searches were performed in the Scientific Electronic Library

Online (SciELO), National Library of Medicine National Institutes of Health (PubMed) and Medical Literature Analysis and Retrievel System Online (MEDLINE) databases. After analyzing the main terminologies, the descriptors selected from the list of Health Sciences Descriptors (DeCS) were: Health promotion. Men's health. Prostate neoplasms.

From this perspective, in order to enable the quality and relevance of this review, full studies published in the last five years in English and Portuguese were included. On the other hand, course completion papers, master's dissertations, doctoral theses, editorials, expert opinions, and restricted-access papers were excluded.

The data analysis was done through the construction and systematization of the most robust results found. To this end, a qualitative investigation of the studies was carried out, with a view to identifying the main trends and gaps in the literature and favoring evidence-based medicine focused on clinical practice.

LITERATURE REVIEW

PROSTATE CANCER

Prostate cancer is a malignant disease resulting from the disordered growth of cells, with morphological, structural and metabolic alterations, as well as accelerated division and genetic mutations. This disease can invade adjacent organs and, in more severe cases, can reach places far from its origin. It is a disease that is usually associated with several triggering factors (Araújo, 2024). Today, it is the second leading cause of death from neoplasia in the male population, a situation that proves its epidemiological importance in the country (Brasil, 2022).

In this scenario, a study carried out in 2022 found that the mortality rate, specifically in the age group of 60 to 69 years, was increasing between 2000 and 2009. However, it was not enough to change the general trend of stability observed throughout the series. Five-year specific survival was 79.6% and had a negative association with age, with lower survival from seventy years onwards (Evangelista et al., 2022).

A study carried out in the United States, whose sample consisted of 24,054 patients, using the Surveillance Epidemiology and End Results Program (SEER) database, observed that the worst survival results were found in men aged 65 years or older and that mortality was related to age, marital status, race, Gleason score, stage and treatment approach (Zheng et al., 2020).

The prostate is an exocrine gland that is part of the male reproductive system. It is located anterior to the rectum and inferior to the bladder, surrounding part of the urethra. It has the function of producing and secreting prostatic fluid, whose alkaline pH favors the

locomotion of spermatozoa. When it unites with the secretion of the seminal vesicles and sperm in the urethra, it forms semen (Almeida et al., 2021).

In childhood, the prostate is relatively small. At puberty, due to the stimulation of testosterone, it begins to grow. Around the age of twenty, it reaches its maximum size and remains so until the age of fifty. After this age, regression occurs because of the decrease in testosterone. Testicular androgens act on the growth and survival of prostate cells. Thus, castration triggers gland atrophy resulting from diffuse apoptosis (Brito et al., 2024).

Often, three pathological processes affect the prostate: i) inflammation, ii) benign nodular enlargement, and iii) tumors. Of these, benign nodular enlargements are the most prevalent and occur a lot in advanced age. In view of this, they are often considered as a physiological process specific to aging (Gandaglia et al., 2021).

Prostate histology is composed of a pseudo-stratified epithelium, which has three subtypes: luminal, basal and neuroendocrine. Thus, according to recent studies, cancers of luminal origin are the most aggressive. There are also fibroblasts, smooth muscle fiber and autonomic nerve, vascular endothelium, defense cells, and lymph nodes, which can exhibit a varied type of behavior depending on the aggressiveness of the disease (Nascimento et al., 2022).

Some prostate tumors can grow abruptly, spreading to other organs, whose outcome is death. However, most develop insidiously (it takes an average of fifteen years to reach 1 cm^3). Therefore, it does not manifest signs during life or threaten men's health (Pereira et al., 2021).

When it spreads to other sites, the most common site of metastasis is the axial skeleton, and most of the time, osteoblastic lesions are observed. In addition, in descending order of frequency, the most affected regions are the lumbar spine, proximal femur, pelvis, and thoracic spine (Sekhoacha et al., 2022).

In this context, local spread harms periprostatic structures, such as the seminal vesicles and the base of the bladder. The lymphatic lymph nodes first affect the obturator lymph nodes, and later, the para-aortic lymph nodes. Hematogenous has a predilection for the axial skeleton, but the involvement of long bones and other organs and tissues is also common (Porcacchia et al., 2022).

In addition, prostate cancer is not unique and also does not occur identically in all men. Each typology has its own natural history and evolution. Therefore, in the same organ there can be several malignant tumors of the same lineage with different degrees of aggressiveness, characteristics, severity, and forms (Silva et al., 2021).

In this sense, according to Silva et al. (2021), there are five types of prostate cancer, namely:

Adenocarcinoma: it is the most common. It occurs with the abnormal proliferation of cells, which originates directly in the glandular tissue of the prostate.

Sarcoma: it is rare. It is not only found in old age, it can also occur in young adults and even children, and can appear in soft tissues and bone.

Neuroendocrine Tumor: in addition to being very aggressive, it is rare. It secretes atypical substances and accelerates disordered growth, which originates in the endocrine and neural cells of the affected tissue.

Carcinoma: occurs in any organ of the body. It appears in the epithelial tissue that surrounds the skin and various organs, including the prostate.

Transitional Cell Carcinoma: more specific. It damages the epithelium that covers the urinary system, being more prevalent in the bladder and prostate.

Because of the multiple modes of clinical presentation, the variable extent of the disease, the diverse architecture, and the unique cytological characteristics, several prognostic and staging factors have been described. As an example, the Whitmore system was one of the first, and is still useful in some organizations (Fontes et al., 2022).

There is also the Gleason score, which is the most used today. In this system, tissue cytoarchitecture is classified into five grades, with 1 being the best differentiated and 5 being the least differentiated. The others are intermediate between these two extremes. Also, the prognosis of each person can also be evidenced through the TNM classification (tumor, lymph node, and metastasis) (Oliveira et al., 2021).

Adenocarcinoma affects the posterior and lateral regions of the peripheral area of the prostate, being heterogeneous in 50% of cases. It often extends to the apex. Its prognosis is associated with some histopathological data, such as topography/laterality, tumor volume/size, type, degree of differentiation, presence of capsular and extraprostatic neoplastic invasion, state of surgical margins, and presence of metastases in regional or distant lymph nodes (Medeiros et al., 2023).

DIAGNOSIS OF PROSTATE CANCER

Among the control actions for prostate cancer, timely detection stands out and is divided into two actions: early diagnosis and screening, also called screening. The first identifies the disease in early stages in people with signs and symptoms. The second individuals are asymptomatic. These two strategies differ in terms of indications,

implementation criteria, and associated risks, in order to favor the chances of cure and reduce morbidity and mortality (Gandaglia et al., 2021).

Prostate cancer screening can be done with digital rectal examination and with serum prostate-specific antigen (PSA) dosage. Such conducts are recommended from the age of 45 for individuals with risk factors and 50 years for those who do not. However, there is no consensus among experts on this strategy, since this neoplasm, in most cases, grows indolently and does not show signs during life or threaten men's health. Although it can grow quickly and spread to other organs and cause death (Santos et al., 2022).

In this sense, a study carried out in 2021 found that, in all age groups, the incidence of prostate cancer began to decline in 2008, with the biggest drop between 2011 and 2012, a situation that can be associated with the reduction in PSA performance (Sung et al., 2021).

Also, a study carried out in 2024 showed that digital rectal findings associated with the PSA result may suggest the existence of the disease. In these cases, multiparametric magnetic resonance imaging is indicated in order to visualize suspicious lesions in the prostate (Brito et al., 2024).

On the other hand, Junior et al. (2023) point out that all men should perform PSA from the age of forty, and if necessary, do digital rectal examination, ultrasound via abdominal, transrectal, biopsy, tomography, magnetic resonance imaging, and bone scintigraphy. These tests can help in early diagnosis and determine the effectiveness of treatment, since prostate cancer is a silent and potentially curable disease (Silva et al., 2021).

Thus, abdominal ultrasound is the most used exam as the first choice in cases of suspected prostate anomalies. Transrectal ultrasound, despite providing more accurate information, is indicated only in the case of the need for biopsies, the result of which is given by means of the Histological Grading of the Gleason System, to evaluate the possibility of metastasis, since it is a heterogeneous neoplasm. Thus, the same tumor may present regions of greater and lesser cell differentiation (Taplin; Smith, 2022).

Despite the lack of consensus, prostate cancer screening is widespread, even though the best available evidence demonstrates an imbalance between risks and possible benefits. Routine PSA and/or digital rectal examination in asymptomatic individuals is associated with many diagnoses and is accompanied by notable damage to men's quality of life (Santos et al., 2022).

This damage is due to false-positive results, which may require a biopsy, triggering pain, bleeding, and infection. In addition, overdiagnosis and overtreatment can result in

erectile sexual dysfunction, urinary incontinence, in addition to emotional effects for both men and their families (Coylewright et al., 2020).

From this perspective, the World Health Organization and the Brazilian Ministry of Health do not recommend population-based screening for prostate cancer. However, it emphasizes the strengthening of educational and communication actions in health on self-care and prevention of chronic non-communicable diseases (Who, 2020).

Based on this, the National Cancer Institute, since 2008, has recommended that screening should only be done in men who spontaneously demand these exams and after a shared decision-making process, which takes into account the risks and benefits. As an alternative, it is suggested to control the disease through the training of professionals, organization of care, clarification to the population, and agility in the diagnosis confirmation and treatment of cases (Biondo et al., 2020).

Nevertheless, in clinical practice, it is observed that, in most cases, men only seek care when the disease is already installed, with greater chances of complications and early deaths. Because of this, it is of fundamental importance to include the male population in the health-disease process, so that the strong social and cultural influence rooted over the years and generations can give way to protagonism in health (Leal et al., 2023).

The lack of adherence of the male population to primary care and the limitation of specialized services not only hinder the control of this disease, but also highlight the need to make improvements in actions related to comprehensive care for men's health. In this way, strategies aimed at health education can contribute to the transformations of preventive care practice, as well as favor the perception of relevance and protagonism (Biondo et al., 2020).

CLINICAL MANIFESTATIONS OF PROSTATE CANCER

In the initial phase, prostate cancer has a silent evolution. As a result, many patients do not manifest any symptoms. When they develop, these are similar to those of benign prostate growth. However, the first clinical manifestations may appear during local growth, due to the tumor compressing the urethra. In this case, there is urinary retention, decreased urine stream, and frequency (Silva et al., 2021).

Soon after, cancer symptoms may appear invading neighboring organs, such as the bladder (hematuria) or rectum (hematochezia and rectal pain), and eventually, the lymph nodes of the pelvis (edema of the legs) and abdomen (abdominal pain). Most distant metastases occur in the bones, especially the spine, hip, and ribs, which can cause

localized pain in these areas. In more advanced cases, the disease can cause weakness, anemia, hyporexia, generalized infection, and kidney failure (Prado et al., 2020).

Involvement of the spine can trigger an epidural compression syndrome (paraplegia, sensory level, and sphincter disorder). Eventually, the diagnosis will be established through symptoms related to visceral metastases. These latter manifestations, in turn, are common in the terminal stages of the disease, especially when there is refractoriness to androgen deprivation therapy (Porcacchia et al., 2022).

Tumors identified by digital rectal examination are almost always relatively large, with a greater chance of advanced disease. This exam only detects more peripheral lesions, which are located on the lateral and/or posterior surfaces of the gland. However, in 25-35% of cases, this neoplasm is identified in other topographies. Therefore, it ends up not being noticed during the procedure (Takemura et al., 2022).

The PSA test is "prostate-specific" and not "cancer-specific". Thus, it is an exclusive laboratory marker of damage to the prostatic epithelium. Because of this, it increases not only in the presence of neoplasia, but also in benign conditions. In this case, it is usually kept between 4-10 ng/ml. On the other hand, values > 10 ng/ml are more specific for malignancy, and > 100 ng/ml predict the existence of metastasis with great accuracy. Thus, the follow-up of serum PSA levels is relevant to monitor the response to treatment (Brito et al., 2024).

TREATMENT OF PROSTATE CANCER

The most important aspects to guide the therapeutic approach in prostate cancer are the extent of the disease and the patient's clinical condition. The disease restricted to the gland is potentially curable with aggressive treatment, and younger individuals with fewer comorbidities are those who can actually benefit from cure, since the evolutionary course of most prostatic neoplasms is quite long (Fontes et al., 2022).

Thus, the treatment of prostate cancer encompasses the combination of surgery, radiotherapy, and chemotherapy. However, drug resistance, complications and adverse effects are common, and therefore, the therapy instituted is often not able to reduce mortality rates, remaining below the ideal. The choice of therapy is based on the patient's life expectancy, PSA, Gleason score, disease stage, comorbidities, side effects, and individual preference (Bravo et al., 2022).

Some of these criteria, especially the PSA value, the Gleason score, and the stage of the disease, allow patients to be stratified into categories according to the possibilities of

cure. For localized neoplasia, the two treatment modalities for primary therapy are surgery and radiotherapy, both with good results (Silva et al., 2021).

In this scenario, radical prostatovesiculectomy, also called laparoscopic radical prostatectomy, represents the main form of curative treatment for non-metastatic prostate cancer. Among the variations of existing techniques, retropubic radical prostatectomy (or open surgery) and robotic-assisted radical prostatectomy stand out (Medeiros et al., 2023).

Robotic-assisted radical prostatectomy contemplates maintaining the benefits of minimally invasive surgery and, at the same time, favors cancer control, preserves urinary continence and erectile function, decreases operative time and hospitalization, and reduces blood loss and the duration of bladder catheterization (Medeiros et al., 2023).

As for the treatment of locally advanced disease, the most indicated choices are hormonal blockade aids with prostatovesiculectomy and radiotherapy, as monotherapy is not effective in these cases. In this sense, a study carried out in 2023 pointed out that the use of immunotherapies has proven to be quite effective. However, it can cause toxicity in the endocrinological system, resulting in endocrinopathies, which can be fatal if left untreated (Vilaça et al., 2023).

In view of this, each case must be evaluated individually, in order to decide on the indication, maintenance, or interruption of therapy, define the risks, benefits, and best results, with the aim of offering the best available treatment, preserving the quality of life and autonomy of each patient (Vilaça et al., 2023).

Regarding the treatment of disseminated metastasis, it is known that cure is unlikely. Nevertheless, the therapy includes the suppression of androgens, luteinizing hormones, estrogens, as well as pure or mixed antiandrogens (cyproterone, bicalutamide, nilutamide, and flutamide), and the procedure considered the gold standard is bilateral orchiectomy (Klein, 2021).

In chemotherapy treatment, drugs are used that allow tumor cells to be reached at different stages of the cycle. As a result, there is cell destruction, preventing its development. Thus, the drugs used are docetaxel, cabazitaxel, mitoxantrone, and estramustine. The first and second are cytostatic agents that prevent the formation of the mitotic spindle during mitosis. Thus, individuals who are in an advanced stage of the disease should be treated with docetaxel, since, in general, they have metastasis in organs such as the liver and lung. However, it is more frequent in the skeleton (Souza; Lopes, 2020).

In principle, the more advanced the disease is, the lower the chance of cure, since there are no reliable means to establish its natural history, just as there is individual

variation in the prognosis. This means that some III stage tumors will be cured with treatments directed only at the prostate, while those in stage I may evolve with systemic recurrence, depending on the therapy initially indicated (Almeida et al., 2021).

CONCLUSION

Prostate cancer is a malignant disease resulting from the disordered growth of cells, with morphological, structural and metabolic alterations, as well as accelerated division and genetic mutations. This neoplasm can invade adjacent organs and, in more severe cases, can reach places far from its origin. It is a disease that is usually associated with several triggering factors.

From this review, it was possible to identify that despite the lack of consensus, prostate cancer screening is widespread, even though the best available evidence demonstrates an imbalance between risks and possible benefits. Routine PSA and/or digital rectal examination in asymptomatic individuals is associated with many diagnoses and is accompanied by notable impairments to the quality of life of men.

In clinical practice, it is observed that, in most cases, men only seek care when the disease is already installed, with greater chances of complications and early deaths. Because of this, it is of fundamental importance to include the male population in the health-disease process, so that the strong social and cultural influence rooted over the years and generations can give way to protagonism in health.

Finally, future perspectives need to move towards elucidating the etiology of this disease, which, so far, remains unexplained or incompletely understood, in order to obtain more efficient treatments and improve the quality of life of patients affected by this disease.

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