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The present and future of prostate cancer. The importance of physical activity - a comprehensive review of the literature

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Abstract

Introduction: Prostate cancer is one of the most common malignancies affecting men worldwide, which poses a serious health risk due to its high incidence and impact on quality of life. Despite advances in the diagnosis and treatment of this condition, the management of advanced and aggressive forms of the disease remains complex.

Aim of the Study: The aim of this study is to review current diagnostic methods, treatment strategies and prognostic factors in prostate cancer, that a particular focus on personalized medicine and multidisciplinary approaches to improve patient outcomes.

Materials and Methods: A comprehensive literature review was conducted using PubMed sources and other scientific databases, focusing on currently available publications. The literature available in the PubMed database was reviewed using the following keywords: “prostate cancer” “prostate cancer diagnosis”, “prostate cancer treatment”, “personalized medicine for prostate cancer”, “physical activity in prostate cancer”. The review included studies on prostate cancer epidemiology, pathogenesis, advances in diagnosis, treatment, physical activity and future research directions.

Conclusions: Advances in diagnostic technologies and emerging new therapies have significantly improved the prognosis for patients with prostate cancer. However, continued research and commitment to personalized treatment strategies are essential to meet the challenges of advanced disease. Multidisciplinary collaboration and patient-centered care remain key to optimizing outcomes and improving quality of life for prostate cancer patients.

Keywords: prostate cancer, prostate cancer diagnosis, prostate cancer treatment, personalized prostate cancer medicine, physical activity and sports in prostate cancer, advanced prostate cancer therapies.

Introduction

Prostate cancer is one of the most common malignancies affecting men worldwide. It is characterised by uncontrolled cell proliferation within the gland and poses a significant health risk due to its high incidence and the possibility of patient metastasis and death[1]. Epidemiologically, the incidence of prostate cancer varies by region, with higher rates reported in developed countries, attributed to better diagnostic capabilities and widespread screening programmes [2]. A comprehensive understanding of prostate cancer pathogenesis, diagnostic

methods and therapeutic approaches is essential to improve patient outcomes and survival rates [3].

Epidemiology

Prostate cancer is the second most commonly diagnosed cancer and the fifth leading cause of cancer deaths among men worldwide. According to the Global Cancer Observatory, there will be approximately 1.4 million new cases and 375,000 deaths from prostate cancer in 2020 [4]. The incidence of prostate cancer shows wide geographic variation, with the highest rates observed in developed regions such as North America, Europe and Australia, and the lowest rates in Asia and Africa[5]. Several factors contribute to geographic differences in prostate cancer incidence. Mainly involve differences in access to health care, availability of screening programs, dietary habits, genetic predisposition and environmental exposures. For example, the increasing
use of prostate-specific antigen (PSA) testing in high-income countries has led to higher detection rates [6]. On the other hand, limited access to health care and screening in low-income regions may result in underdiagnosis and lower reported incidence rates, and thus higher mortality [5]. Age is a major risk factor for prostate cancer, with incidence rates rising sharply in men over the age of 50. The majority of prostate cancer cases are in men 65 years of age and older [2]. Family and genetic factors also play an important role. Men who have a first-degree relative diagnosed with prostate cancer have a two to three times higher risk of developing the disease [7]. In addition, certain genetic mutations, such as those in the BRCA1, BRCA2 and HOXB13 genes, have been found to be associated with a higher risk of prostate cancer [8]. Ethnic and racial differences in prostate cancer incidence and outcomes have been well documented. African-Americans have the highest rates of prostate cancer incidence and mortality compared to other ethnic groups [9]. They are also more likely to be diagnosed with the disease at a younger age and at a more advanced stage. The reasons for these differences are multifactorial, such as genetic susceptibility, socioeconomic status, access to health care and lifestyle factors [10]. Lifestyle factors such as diet, physical activity and body weight have also been linked to prostate cancer incidence. High-fat diets, especially those rich in animal fats (saturated fat), have been linked to an increased risk of prostate cancer [11]. On the other hand, a diet rich in fruits, vegetables and fish may have a protective effect. Regular physical activity and maintaining a healthy body weight are recommended to reduce the risk of prostate cancer

and improve overall health outcomes [12]. The burden of prostate cancer is expected to increase in the coming decades due to an aging population and the increasing adoption of Western lifestyles in developing countries. Public health participation, including awareness campaigns, early detection programs, and access to appropriate treatment, are key to addressing the rising incidence of prostate cancer worldwide [13].

Pathogenesis

The pathogenesis of prostate cancer involves a multifactorial process that includes genetic mutations, hormonal influences and environmental exposures. Understanding these mechanisms is particularly important for developing effective prevention and treatment strategies.

Genetic Factors. Genetic predisposition plays a significant role in the development of prostate cancer. Approximately 5-10% of cases are believed to be hereditary, resulting from mutations in specific genes such as BRCA1, BRCA2 and HOXB13 [8]. [8]. Such mutations can lead to increased cell proliferation and a higher risk of malignant transformation. For example, BRCA2 mutations are associated with a 20-fold increased risk of developing prostate cancer[14]. In addition, genome-wide association studies (GWAS) have identified several single nucleotide polymorphisms (SNPs) associated with increased prostate cancer risk [15].

Hormonal Influences. Androgens, mainly testosterone and dihydrotestosterone (DHT), play a key role in the development and progression of prostate cancer. The androgen receptor (AR) signaling pathway affects the growth and differentiation of prostate cells. Abnormal activation or overexpression of AR can promote tumor cell proliferation[16]. Therapies targeting androgen deprivation are commonly used to treat advanced prostate cancer, emphasizing the importance of hormonal regulation in the progression and subsequent treatment of the disease [17].

Molecular Pathways. Several key molecular pathways are involved in the pathogenesis of prostate cancer. These include the PI3K/AKT/mTOR pathway, which is involved in cell growth and survival, and the RAS/RAF/MEK/ERK pathway, which regulates cell proliferation and differentiation [18]. Alterations in these pathways can lead to uncontrolled cell division and

tumor growth. For example, loss of the tumor suppressor PTEN, which negatively regulates the PI3K/AKT pathway, is often observed in this cancer[19].

Environmental and Lifestyle Factors. Environmental exposures and lifestyle factors also contribute to an increased risk of prostate cancer. Diets high in saturated fat and red meat have been linked to an increased risk of prostate cancer, while diets rich in fruits and vegetables may have a protective effect [11]. Obesity and physical inactivity are additional risk factors that can affect inflammatory processes and hormone levels, further contributing to cancer development [20]. Chronic inflammation within the prostate, often caused by infections or other irritants, has been put forward as a potential mechanism of carcinogenesis [21].

Epigenetic Modifications. Epigenetic changes, such as DNA methylation and histone modification, play an important role in regulating gene expression without altering the DNA sequence. Abnormal epigenetic modifications can result in silencing of tumor suppressor genes and activation of oncogenes, contributing to prostate cancer progression [22]. For example, hypermethylation of the GSTP1 gene promoter is a common epigenetic change observed in prostate cancer [23].

Interactions Between Factors. The interplay of genetic, hormonal, environmental and epigenetic factors underscores the complexity of prostate cancer pathogenesis. Genetic predisposition can be modulated by environmental exposures and lifestyle choices, while hormonal changes and epigenetic alterations can influence the behavior of genetically altered cells. This multifactorial nature of prostate cancer demonstrates the need for a comprehensive approach to understanding and treating the disease.[24]

Diagnosis

Early detection of prostate cancer is important for effective treatment and improved survival outcomes. Various diagnostic methods, ranging from initial screening to advanced imaging and biopsy techniques, are used to detect and evaluate the stage of prostate cancer.

Screening Methods. Prostate-specific antigen (PSA) testing is the most common screening tool used for early detection of prostate cancer. PSA is a protein produced by the prostate gland, and

elevated levels in the blood can indicate the presence of prostate cancer [25]. However, PSA levels can also be elevated due to benign prostatic hyperplasia (BPH) or prostatitis, leading to potential false-positive results [26]. Despite these limitations, PSA testing has been shown to reduce prostate cancer mortality by allowing early detection [6]. Dermal rectal examination (DRE) is another screening method in which a physician palpates the prostate gland through the rectum to detect abnormalities such as nodules, hypertrophy or asymmetry [27]. Although DRE testing alone is less sensitive than PSA testing, it can provide additional information, especially when combined with PSA testing.

Imaging Techniques. Advances in imaging technologies have improved the detection and staging of prostate cancer. Multiparametric magnetic resonance imaging (mpMRI) combines anatomical and functional imaging to provide detailed information about the prostate and surrounding tissues[28]. MpMRI is particularly useful for identifying suspicious areas within the prostate that may require further evaluation through targeted biopsy. Transrectal ultrasound (TRUS) is commonly used during prostate biopsy to properly guide needle placement. TRUS can also help detect prostate abnormalities, but is less sensitive than mpMRI in detecting clinically significant cancer [29]. Other imaging modalities, such as computed tomography (CT) and positron emission tomography (PET), are used to determine staging and detect metastases [30].

Biopsy Techniques. Prostate biopsy remains the gold standard for prostate cancer diagnosis. During a biopsy, small samples of tissue are taken and histologically examined for the presence ofcancer cells. There are several biopsy techniques:

Systematic biopsy under TRUS guidance. This traditional method involves taking multiple tissue samples from different areas of the prostate gland under ultrasound guidance [31]. Although widely used, it can miss clinically significant tumors and detect insignificant lesions.

MRI-guided biopsy. Combining mpMRI with TRUS (fusion biopsy) allows targeted sampling of suspicious areas identified on MRI, improving the detection of clinically significant prostate cancer [32].

Biomarkers and Molecular Testing.

In addition to PSA, several other biomarkers and molecular tests are being investigated to improve the accuracy of prostate cancer diagnosis. Tests such as the Prostate Health Index (PHI) and 4Kscore combine multiple biomarkers to better stratify prostate cancer risk and reduce unnecessary biopsies [33]. Genetic and genomic tests, such as Oncotype DX and Decipher, analyze the expression of specific genes associated with prostate cancer aggressiveness to help with risk stratification and treatment selection decisions [34].

Risk Stratification.

Accurate risk stratification is essential for making decisions about treatment choices. The Gleason scoring system, based on histologic classification of prostate cancer cells, remains a key tool for assessing tumor aggressiveness [35]. In addition, clinical stage, PSA levels and imaging findings are integrated with risk models to classify patients into low-, intermediate- or high-risk categories [36].

Continued advances in diagnostic techniques and the invention of new biomarkers are improving early detection and risk stratification of prostate cancer, ultimately improving patient outcomes and personalized treatment approaches.

Treatment Methods

Treatment options for prostate cancer vary depending on the current stage of the disease, the patient's overall health and personal preferences. Primary treatment options include active surveillance, surgery, radiation therapy, hormone therapy and new treatments such as immunotherapy and targeted therapies.

Active Surveillance. Active surveillance is a management strategy for men with localized low-risk prostate cancer. It involves close monitoring of the patient's condition without immediate intervention, deferring treatment until there are signs of disease progression [37]. This approach minimizes potential side effects associated with more aggressive treatments and is appropriate for patients with low PSA levels, low Gleason score and limited tumor volume [38]. Regular PSA, DRE and periodic biopsies are essential components of active surveillance [39].

Surgery. Surgical removal of the prostate, known as radical prostatectomy, is a common treatment for localized prostate cancer. The procedure can be performed using traditional open surgery, laparoscopic techniques or da Vinci robot-assisted methods [40]. Robotic-assisted laparoscopic prostatectomy (RALP) has gained popularity due to its minimally invasive nature, less blood loss and shorter recovery time after surgery [41]. However, all surgical options carry risks, including urinary incontinence, erectile dysfunction and potential complications related to anesthesia [42].

Radiation Therapy.

Radiation therapy uses high-energy rays to target and kill cancer cells. There are two main types of radiation therapy for prostate cancer:

External Beam Radiation Therapy (EBRT). This method involves directing radiation from outside the
body toward the prostate. Techniques such as intensity-modulated radiation therapy (IMRT) and image-guided radiation therapy (IGRT) increase precision and minimize damage to surrounding healthy tissue [43].

Brachytherapy. It involves placing radioactive seeds directly into or near the prostate tumor. Brachytherapy can be used alone for low-risk tumors only, or in combination with EBRT for higher-risk cases [44].

Both types of radiation therapy can cause side effects, including bowel and urinary problems, as well as erectile dysfunction[36].

Hormone Therapy.

Hormone therapy, also known as androgen deprivation therapy (ADT), is designed to lower levels of male hormones (androgens) that can fuel prostate cancer growth. ADT can be achieved through surgical castration (orchiectomy) or testosterone-lowering drugs [45]. Drugs used in ADT include luteinizing hormone-releasing hormone (LHRH) agonists and antagonists, as well

as anti-androgens [46]. Hormone therapy is often used in advanced or metastatic prostate cancer, either alone or in combination with other treatments[47]. Long-term use of ADT can lead to side effects such as bone thinning, hot flashes and metabolic changes[48].

Immunotherapy and Targeted Therapies.

New treatments such as immunotherapy and targeted therapies offer new hope for patients with advanced prostate cancer.

Immunotherapy. Sipuleucel-T is an FDA-approved immunotherapy for metastatic castration-resistant prostate cancer. It relies on modifying a patient's immune cells to attack prostate cancer cells [49]. Other immunotherapeutic approaches, including checkpoint inhibitors, are currently under investigation [50].

Targeted Therapies. These therapies focus on specific molecular targets involved in tumor growth.
PARP inhibitors, such as olaparib, have shown promise in treating prostate cancer with specific genetic mutations (e.g., BRCA1/2) [51]. In addition, targeted radioligand therapy using agents such as 177Lu-PSMA-617 is being investigated for advanced prostate cancer [52].

Multimodal Approaches.

Combining different treatment modalities can increase the effectiveness of therapy. For example, combining radiation therapy with hormone therapy has been shown to improve outcomes for localized high-risk prostate cancer [53]. Multimodal approaches are tailored to individual patient profiles and disease characteristics, emphasizing the importance of personalized treatment plans [54]. Ongoing research and clinical trials continue to refine and expand treatment options for prostate cancer, aiming to improve survival rates and quality of life for patients.

Physical activity and sports

Regular physical activity and sports play an important role in the prevention, treatment and rehabilitation of prostate cancer. Numerous studies show that exercise can have a beneficial effect on both the risk of prostate cancer and the outcome of patients diagnosed with the disease.

Prevention.

Epidemiological studies suggest that regular physical activity is associated with a reduced risk of prostate cancer. Exercise can help lower risk by improving immune function, reducing inflammation and lowering levels of certain growth factors and hormones, such as insulin-like growth factor (IGF) and testosterone, which can promote cancer growth [55]. In addition, physical activity helps maintain a healthy body weight, which is important because obesity is a known risk factor for prostate cancer [56].

Prevention during treatment.

For patients undergoing treatment for prostate cancer, physical activity may mitigate some of the adverse effects associated with therapies such as hormone therapy, radiation therapy and chemotherapy. Exercise has been shown to reduce fatigue, improve muscle strength, increase cardiovascular fitness and promote mental health [57]. In particular, resistance training can counteract muscle loss and reduced bone density, which are common side effects of androgen deprivation therapy (ADT) [58].

Rehabilitation after treatment.

After treatment, physical activity can take part in rehabilitation and improve quality of life. Regular exercise can help alleviate lingering side effects, such as incontinence and sexual dysfunction, and reduce the risk of cancer recurrence [59]. Engaging in a structured exercise program can also help patients regain physical fitness and mental well-being, contributing to better overall recovery [60].

Exercise Recommendations and Safety.

Patients with prostate cancer should consult with their physician before starting a particular exercise program. Tailored exercise recommendations should take into account the patient's fitness level, medical history and any comorbidities [61]. Supervised exercise sessions, especially in the early stages, can help ensure safety and proper technique, reducing the risk of injury [62].

Prognosis and Survival rates

Prognostic factors and survival rates for prostate cancer vary depending on the stage of the disease at diagnosis, the aggressiveness of the cancer and the patient's overall health. Early detection of the disease and advances in treatment have significantly improved survival rates for prostate cancer patients.

Prognostic Factors. Prognosis of prostate cancer is affected by several key factors:

1. Stage at Diagnosis. The degree of cancer spread at the time of diagnosis is one of the most important prognostic factors. Localized prostate cancer, confined only to the prostate gland, has a much better prognosis compared to advanced stages in which the cancer has spread to distant organs [1].

2. Gleason Score. The Gleason scoring system assesses the aggressiveness of prostate cancer based on the histologic appearance of tumor cells. A higher Gleason score is associated with more aggressive cancer and thus a worse prognosis [35].

3. PSA Levels. Prostate-specific antigen (PSA) levels at diagnosis and changes in PSA levels over time (PSA velocity) can provide important prognostic information. Higher PSA levels and rapid PSA rise are often associated with higher risk of progression and worse outcomes [63].

4. Lymph Node Involvement. The presence of cancer in the lymph nodes indicates a more advanced stage of the disease (metastasis) and is associated with a worse prognosis [64].

5. Genetic Factors. Certain mutations and genetic alterations, such as BRCA1/2 mutations, are associated with more aggressive forms of prostate cancer and may negatively affect prognosis [8].

Survival Rates.

Survival rates for prostate cancer have improved significantly over the past few decades, largely due to advances in early detection and treatment. According to the latest statistics:
- The relative 5-year survival rate for localized and regional prostate cancer is nearly 100%[65].
- The relative 10-year survival rate for all stages combined is about 98% [66] .
- For metastatic prostate cancer, the 5-year relative survival rate drops to about 30% [1].
These statistics underscore the importance of early detection and effective treatment strategies to improve outcomes for prostate cancer patients.

Impact of Treatment Advances.

Advances in the treatment of prostate cancer, such as the development of new surgical techniques, radiation therapy, hormonal therapy and targeted therapies, have contributed to improved survival rates. For example, the introduction of robot-assisted surgery has reduced complications and shortened recovery times [41]. Similarly, new radiation therapy techniques, such as intensity-modulated radiation therapy (IMRT) and proton beam therapy, offer more precise targeting of cancer cells while sparing healthy tissue [67].

Quality of Life Considerations.

While survival rates are a priority, quality of life is also an important factor for prostate cancer patients. Treatment can have significant side effects, including urinary incontinence, erectile dysfunction and bowel problems, which can affect patients' overall well-being [68]. Therefore, a key goal in prostate cancer treatment is to balance effective cancer control with minimizing therapy-related side effects.

Future Directions.

Ongoing research focusing on identifying new biomarkers to better stratify risk, developing more effective and less invasive treatments, and understanding the genetic and molecular basis of prostate cancer to develop personalized treatments. Clinical trials continue to play an important role in advancing our knowledge and improving outcomes for prostate cancer patients[54].

Conclusions

Prostate cancer remains an important health issue due to its high incidence in the population and significant impact on patients' quality of life. Early diagnosis and advances in treatment methods have significantly improved the prognosis for many patients. However, there is a need for further research in identifying new biomarkers, developing more precise diagnostic methods and targeted therapies. Personalized treatment, taking into account individual genetic and molecular characteristics, represents the future of prostate cancer care. Successful treatment of this disease requires a multidisciplinary approach, combining the latest scientific advances with comprehensive patient care.

Author's contribution

Conceptualization, Tomasz Kucharski; methodology, Tomasz Kucharski and Julita Gmitrzuk; software, Martyna Opatowska and Joanna Jakubiec; check, Katarzyna Wiśniewska and Marta Piotrowska; formal analysis, Tomasz Kucharski and Zuzanna Malinka; investigation, Tomasz Kucharski and Anna Jachymek; resources, Martyna Opatowska and Julita Gmitrzuk; data curation, Joanna Jakubiec, Katarzyna Wiśniewska; writing – rough preparation, Tomasz Kucharski; writing - review and editing, Tomasz Kucharski and Marta Piotrowska; visualization, Tomasz Kucharski, Zuzanna Malinka and Anna Jachymek; supervision, Katarzyna Wiśniewska and Julita Gmitrzuk; project administration, Tomasz Kucharski and Marta Piotrowska. All authors have read and agreed with the published version of the manuscript.

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