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AGING: A SYSTEMATIC REVIEW ON THE CORRELATION BETWEEN GERIATRIC DISEASES AND PROSTATE CANCER

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ABSTRACT

Prostate malignancy is a frequent carcinoma and is the 2nd common in adult males accounting for about 3.8% of all cancer mortality in men in 2018; this has been linked to older men around 70 years old (≥70). About 2,293,818 new diagnoses are anticipated by 2040, considering the disparity in Social, environmental, and genetic factors, which also has a significant role in this disease. Geriatric syndromes are clinical state and are mostly common in elderly people, especially frail older adults; these conditions are not always associated with a certain underlying disease. The study aims to give a brief review of Prostatic Carcinoma, Geriatric diseases and also discuss the correlation between aging and prostate malignancy. As obtained from different studies, malignancy is primarily a disease of older adults, with patients over 65 accounting for most cancer diagnoses and deaths. The elongation of life is a significant challenge related to more medical conditions, and due to an increase in lifespan, the figure of elderly patients with prostate malignancy will increase. It was concluded that as we emerge from the baby boomer generation, the figure of elderly males with prostate malignancy will keep increasing. However, comprehensive geriatric evaluation and pertinent disease staging at diagnosis will aid adequately manage these patients. This method will assist us in recommending the best course of action, focusing on maintaining the quality of life.

***Keywords*:** Geriatric diseases, Prostate, Aging

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1. INTRODUCTION

Aside from lungs malignancies, prostate malignancy is the second mostly frequent carcinoma in males. Over 358,989 deaths and 1,276,106 recent cases in 2018 were attributed to cancer, as mentioned earlier (Bray et al. 2018; Ferlay et al. 2019). Its death rate increases with age (sixty-six years is the average). Black males are more prone to prostate malignancy than white males (Panigrahi et al. 2019). This is related to social, environmental, and genetic differences. In 2040, more than 2,293,818 new cases should be anticipated (Ferlay et al. 2019). During the early stages of prostate cancer, it usually presents with no symptoms requiring little or no treatment. Patients with prostate cancer usually complain of increased frequency of urination, difficulty urinating, and nocturia, which can be caused by prostatic hypertrophy, with the axial skeleton as the most common area of bone metastases. A more severe stage of this disease can be accompanied by urinary retention and back pain. It is predicted that in 2021, Prostatic carcinoma would account for 26% of new non-cutaneous cancer cases and 11% of cancer-related fatalities in the United States (Siegel et al. 2021). In an analysis by Marybeth et al. (2020), Prostate cancer incidence and mortality rates are declining or stabilizing in most countries in most recent years, with the declines more pronounced in high human development countries. These trends may reflect a decline in PSA testing (incidence) and improvements in treatment (mortality).

2. Histology of The Prostate Cancer

The myoelastic/fibromuscular stroma, which is characterized by clusters of smooth muscles combined with elastic fibers, is the distinctive histological characteristic of the prostate. This encircles the parenchyma and glandular tissue of the prostate, which produces around 27% of the seminal fluid.

Prostatic glands release an acidic mixture of enzymes (prostate-specific antigen (PSA), prostatic acid phosphatase, fibrinolysin, and amylase), citric acid, and zinc into the prostatic sinuses in response to the hormone 5-hydroxytestosterone (DHT) (grooves lateral to the luminal aspect of the seminal colliculi). Size-variable prostatic glands feature folds of connective tissue lining their lumens. The connective tissue folding gives the acini an

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extremely atypical appearance. Often, simple columnar or pseudostratified epithelium lines them. Moreover, prostatic concretions (precipitations of prostatic glandular secretions) can be seen in the prostatic gland lumen and are an indication of the patient's age because their frequency rises with advancing years. Another important histological characteristic of the prostate is the presence of the prostatic urethra. The verumontanum gives it a horseshoe shape, and the heavily folded transitional epithelial layer gives it epithelial projections. The ejaculatory ducts and the prostatic utricle (a blind ending duct along the midline of the verumontanum) can also be seen within the prostate's stroma, which is located posterior to the concavity of the prostatic urethra.

3. Diagnosis/Histopathology of Prostate Cancer

To be able to diagnose prostatic carcinoma, the prostate-specific antigen level must be elevated, usually greater than 4mg/mL. However, because a high PSA level is usually seen in older males, a biopsy may also be performed by removing tissue to confirm the presence of cancer. According to a recent systematic analysis, ethnicity contributes significantly to heterogeneity when determining age-adjusted PSA reference ranges, and it should be taken into account when clinically determining PSA levels (Matti et al. 2022). Extra-prostatic gland spread and the presence of perineural invasion, collagenous micronodules, and glomeruloid intraglandular projections inside the prostate are histological characteristics that have been deemed specific for a prostatic cancer diagnosis (Baisden et al. 1999).

Ectopic benign prostatic glands have been discovered in many anatomic sites outside the prostate, including the testis, epididymis, bladder, penile urethra, seminal vesicle, root of the penis, subvesical space, retrovesical space, pericolonic fat and submucosa, perirectal fat, urachal remnant, and spleen. Prostatic glands outside the prostate are typically indicative of cancer (Humphrey 2003).

The defining feature of prostatic carcinoma is perineural invasion. Perineural invasion affects whole prostate glands in the great majority of cases, with literature estimates ranging from 84% to 94% (Byar and Mostofi 1972; Bostwick 1994). Around 25% of needle core biopsy cases reveal perineural invasion, although only 11% of cases in a screening cohort with smaller, earlier-stage tumors did (Bismar et al. 2003). Because the prevalence drops to as low as 2% in needle biopsy tissue, the diagnostic value of perineural invasion is lowered for little or minimal amounts of carcinoma (1 mm in maximum dimension) (Epstein 1995; Thorson et al. 1998). Yet, the mere existence of prostatic glands next to a nerve does not necessarily indicate cancer. Benign prostate glands may touch or encircle nerves (Ali and Epstein 2005). To identify between benign and malignant perineural epithelium, one should rely on the cytologic characteristics of the epithelial cells surrounding a nerve. Higher grade, volume, and stage intraprostatic lymphovascular invasion are linked to a higher likelihood of biochemical failure, distant metastases, and overall survival following radical prostatectomy (Magi-Galluzzi et al. 2011; Fajkovic et al. 2016). Using CD31 or podoplanin (D2-40) antibodies in immunohistochemistry for endothelial cells may be necessary to distinguish between true lymphovascular invasion and artifactual separation of malignant glands from stroma, cancer impingement on vascular spaces, and displacement of benign glands into lymphovascular spaces (Kryvenko and Epstein 2012).

Prostatic epithelial cell invasion of the lymphovascular space can also be considered a specific indicator of malignancy. In needle core tissue, however, this discovery is uncommon. In situations of radical prostatectomy, lymphovascular invasion can be seen in 5% to 53% of patients.

Microscopic clusters of hyalinized stroma known as collagenous micronodules, often referred to as mucinous fibroplasia, are a unique reaction to invasive prostate cancer (McNeal et al. 1991; Bostwick et al. 1995; Baisden et al. 1999). They frequently, but not always, have high mucin production. The micronodules are paucicellular and primarily made of collagen, with a few elongated fibroblastic nuclei visible. True nodules, vaguely lobulated masses, and streaks and strands of the collagenous tissue inside mucinous pools are all possible forms of the collagen. Micronodules can be found both inside glandular lumina and in the stroma next to adenocarcinomatous glands. Collagenous micronodules appear to be extremely specific for carcinoma when used for diagnostic purposes, but their overall diagnostic utility is somewhat constrained given that they are only present in 1–2% of carcinoma-positive needle biopsies (Bostwick et al. 1995; Thorson et al. 1998; Varma et al. 2002) and 13–22% of carcinomas in whole glands in radical prostatectomy specimens (Bostwick et al. 1995; Kaleem et al. 1998). They are linked to adenocarcinomas with the Gleason pattern 3 or 4 (Kim et al. 2015).

Prostatic adenocarcinoma acini include renal glomerulus-like epithelial clumps known as glomerulations (Baisden et al. 1999). It is believed that this intraluminal epithelial development pattern is unique to cancer (Pacelli et al. 1998). The presence of glomerulations in just 3%-15% of needle biopsies with cancer and 5% of radical prostatectomies with adenocarcinoma slightly limits their diagnostic utility (Pacelli et al. 1998; Varma et al. 2002). When viewed under a microscope, glomeruloid entities have tufts or buds that are rounded to ball-like and develop into tiny to medium-sized malignant glands. Typically, the glomeruloid bodies make only a small portion of the cancer. They exhibit a strong Gleason pattern 4 (Epstein et al. 2016b).

Today, immunohistochemistry with antibodies against basal cells (34E12 and p63) and -methylacyl-CoA racemase, or AMACR (also known as P504S and racemase), is the most useful supplementary method for the diagnosis of prostate cancer (Hameed and Humphrey 2005; Brimo and Epstein 2012; Epstein et al. 2014b).

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Monoclonal antibody 34E12, which binds to high-molecular-weight cytokeratins expressed in the cytoplasm of basal cells but not luminal cells, and an antibody against p63, which is confined to basal cell nuclei, are used in the best-studied basal cell immunostains. You can also employ cytokeratin 5/6 to identify basal cells. The sensitivity of basal cell detection seems to be increased by a combination of p63 and 34E12 antibodies (Zhou et al. 2003a).

It's critical to understand that some benign glands may lack or have a discontinuous basal cell layer. Atrophy, one of the benign conditions that is most frequently mistaken for cancer, can, in up to 25% of cases, show scattered basal cell-negative glands (Hameed and Humphrey 2005). Moreover, in atypical adenomatous hyperplasia (adenosis), 50% (range: 10 to 90%) of the glands do not stain basal cells on average. Hence, immunohistochemistry's detection of a broad absence of basal cells in the problematic glands is most supportive of an adenocarcinoma diagnosis when used in the proper histological context. The last type of invasive adenocarcinoma is extremely uncommon, has a unique molecular makeup, and is p63 immunoreactive yet negative for high molecular weight cytokeratins (Osunkoya et al. 2008a; Giannico et al. 2013; Tan et al. 2015).

In addition, the most popular histological stain, hematoxylin and eosin (H&E), offers one of the most crucial cancer diagnostics. (Chan 2014; King and King 2018). H&E-stained tissues provide pathologists with a wealth of information that aids in diagnosis, prognosis, and therapy response prediction (Cottrell et al. 2018; Rakaee et al. 2018; Stein et al. 2019).

A review by Ilic et al. (2013) identified five relevant studies, comprised of 341,342 participants in total. Two of the studies were assessed to be of low risk of bias, whilst the remaining three had more substantive methodological weaknesses. Meta-analysis of all five included studies demonstrated no statistically significant reduction in prostate cancer-specific mortality (risk ratio (RR) 1.00, 95% confidence interval (CI) 0.86 to 1.17). Meta-analysis of the two low risks of bias studies indicated no significant reduction in prostate cancer-specific mortality (RR 0.96, 95% CI 0.70 to 1.30). Only one study included in this review (ERSPC) reported a significant 21% relative reduction (95% CI 31% to 8%) in prostate cancer-specific mortality in a pre-specified subgroup of men. These results were primarily driven by two countries within the ERSPC study that had very high prostate cancer mortality rates and unusually large reduction estimates. Among men aged 55 to 69 years in the ERSPC study, the study authors reported that 1055 men would need to be screened to prevent one additional death from prostate cancer during a median follow-up duration of 11 years. Harms included overdiagnosis and harms associated with overtreatment, including false-positive results for the PSA test, infection, bleeding, and pain associated with subsequent biopsy.

Therapy of advanced prostate cancer is based on interference with androgen receptor (AR) signaling and androgen deprivation therapy (ADT) has been firmly established as the principal therapeutic approach (Hellerstedt et al. 2002). Unfortunately, all patients ultimately develop resistance to primary ADT (surgical/medical castration) as well as novel hormonal therapies (next-generation ADT), which either suppress the synthesis of extragonadal androgens (e.g. abiraterone) or target the androgen receptor directly (e.g. enzalutamide). In a study by some group of researchers, they devised a single-tube assay to detect AR-V7 splice variants and AR point mutations in CTCs using immunomagnetic cell isolation, followed by quantitative real-time PCR and DNA pyrosequencing and prospectively investigated 47 patients with PSA progression awaiting therapy switch. Comparison of response to newly administered therapy and CTC-AR-status allowed effect size estimation. Nineteen (51%) of 37 patients with detectable CTCs carried AR-modifications. Seventeen patients carried the AR-V7 splice variant, one harbored a p.T878A point mutation and one harbored both AR-V7 and a p.H875Y mutation. They estimated a positive predictive value for response and non-response to therapy by AR status in CTCs of ~94% (Steinestel et al. 2019).

In a study by Ahdoot (2020), a total of 2732 men underwent prostate MRI. Of these patients, 2180 had MRI-visible lesions and underwent combined MRI-targeted and systematic biopsies in the same clinical setting. Among the patients who underwent biopsy, 77 were excluded from the analysis because they had undergone previous treatment. The remaining 2103 men were included in the analysis. The majority (79.3%) of men enrolled in this study had undergone at least one biopsy at an outside institution before study enrollment. Of the men who were included in the analysis, prostate cancer was diagnosed in 1312 (62.4%). Of the men diagnosed with cancer, 404 subsequently underwent radical prostatectomy at our institution. The median time between prostate biopsy and radical prostatectomy was 98 days (interquartile range, 74 to 134).

Ga-68-PSMA PET is increasingly being recognized as a powerful tool for the detection and assessment of metastatic disease burden in prostate cancer. The effect of this in clinical practice is profound, with the results of PSMA PET affecting management in about half of the patients. In the context of increasing published literature, our updated meta-analysis highlights the utility of ^{68}Ga-PSMA PET at low PSA levels after prostatectomy. Pooled analysis of PSMA-avid lesions identified anatomical patterns of ^{68}Ga-PSMA PET-detected metastatic deposits in the primary setting and further in the biochemically recurrent cohort after prostatectomy or radiotherapy (Han et al. 2018). The results of a study by Perera et al. (2020) highlight the excellent sensitivity and specificity of ^{68}Ga-PSMA PET in advanced prostate cancer. Specifically, on a per-patient analysis, the sensitivity and specificity of ^{68}Ga-PSMA PET were 77% and 97%, respectively, following pelvic lymph node dissection at the time of RP. On a per-lesion analysis, sensitivity and specificity were 75% and 99%, respectively.

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Geriatric Syndromes are medical conditions of old individuals, incredibly frail ones. Most times, they are not always associated with any underlying disease. Its etiology is thought to be multifactorial. As one age, the reserve capacity of the organs in the system starts to deteriorate, making them vulnerable to stress inducers. This is essential since malignancies and its therapy are potential physiologic stressors that can heighten or initiate geriatric syndromes. Examples of geriatric syndromes are Depression, Urinary incontinence, Delirium, and Cognitive syndromes.

4. Epidemiology of Prostate Cancer

Its prevalence varies by population and region. Oceania had the highest while North America had the lowest, followed by Europe. Africa and Asia had the lower incidence rate (Ferlay et al. 2019). The incidence rate in men over 65 is nearly 65% (Cancer stat facts 2018). Prostatic Carcinoma is frequently diagnosed among men in Europe and accounted for 24% of all recent cancer diagnosis in 2018 (Epidemiology of prostate cancer Europe 2015). Prostatic carcinoma is the 2nd most frequent form of malignancy in the United States of America (USA) (Cancer stat facts. 2018). According to recent studies, over 20-40% of detected cancer of the prostate in the United States and Europe may be overly diagnosed due to extensive testing of the prostate-specific antigen level (Quinn and Babb 2002). Black Americans and the Caribbean share common genetic makeup, which makes them more susceptible to the growth of malignancies than other racial-ethnic groups. (Kheirandish et al. 2011). In a study by Daniyal et al. (2014), he provided awareness about prostate cancer as well as an updated knowledge about the epidemiology, etiology, diagnosis, and treatment of prostate cancer. According to the study, Prostate cancer is more common in men over the age of 65 years and there are 15% cases with positive family history of prostate cancer Worldwide. However, Prostate cancer incidence is strongly related to age with the highest rates in older man. Globally millions of people are suffering from this disease (Daniyal et al. 2014).

Regarding its mortality rate, it was higher in Central America, then Australia, New Zealand, and Western Europe. (Ferlay et al. 2019). While the smallest rate was found in Asia and Northern Africa (Ferlay et al. 2019). Even though the Prostate Cancer incidence rate is high, most diagnoses are made when the cancer is contained inside the prostate. Furthermore, Table 1 shows the epidemiology of prostate cancer across various countries.

Table 1: Epidemiology of prostate cancer across various countries

Population	Incidence rate	Age (Years)	Study Year	References
Nigeria	182.5 per 100,000	NA	2010	Badmus et al. (2010)
United States of America a. White Americans b. Black Americans	a. 156.7 per 100,000 b. 248.5 per 100,000	ASR	2009	Chun et al. (2009)
Lagos, Nigeria	104.6 per 100,000	≥40 Mean and Median age: 60.8 and 60	2013	Ikuerowo et al. (2013)
Australia/New Zealand	111.6 per 100,000	ASR	2021	Yoshimura et al. (2021)
North America	97.2 per 100,000	ASR		
Worldwide	7.1% of 1,276,106 cases	NA	2018	Bray et al. (2018)
Worldwide	60%	Over 60	2018	SEER cancer statistic review, (2018)
France, Guadeloupe	183.6 per 100,000	ASR	2020	WCRF (2020)
South Africa	68.3 per 100,000	ASR	2019	Wang et al. (2022)
Oceania	101.9 per 100,000	ASR	2012	Hassanipour et al. (2016)
China	89.9 per 100,000	65+	2015	Teoh et al. (2019)
Croatia	173.0 per 100,000	65+	2007	
Japan	43.3	68.9	2008-2013	Yoshimura et al. (2021)
Nigeria	16.42, 16.31 (SS), 4.38 (SW), 0.88 (NC), 5.28 (NW)	65.3	1984-2004	Adeloye et al. (2016)
Lagos, Nigeria	0.38	60.8	2012	

Keys: SS- south south; NW- northwest; NC- north central; SW- southwest; ASR- Age significant rate; ASI- Age significant incidence; NA- not applicable.

5. Correlation Between the Two and Their Mortality Rate

The elongation of life is a significant challenge related to more medical conditions, and due to an increase in lifespan, the number of elderly patients with prostatic carcinoma will increase. As discovered by research, prostate malignancy mainly occurs in older males who are between 70 years old (≥70) (Catherine et al. 2004). The research of Mario et al. (2003) in the test result carried out for ages >60 and ≤90 years explains that the Prostatic Specific Antigen (PSA) value went up above the standard upper limit for almost a third of the patients over 60 years (Mario

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et al. 2003) which establishes that prostate cancer should be considered an age-associated disease rather than an aging-related disease.

Catherine et al. (2004) further describes the study of minimal Geriatric Assessment Study; the result shows that of 60 proposed diagnosis prostatic carcinoma patients with a median age of 78 years (between ages 68- 92 years), the result had 46 patients with metastatic prostatic carcinoma and 5 with locally progressed disease with high PSA level without evidence of metastasis. It explains the correlation of geriatric disease to prostate cancer as there has been a surge in the figure of the latest analysis of prostatic carcinoma since the detection of the PSA procedure according to Mario et al. (2003).

It is conclusive that as we emerge, the baby boomer generation, between the ages 65 to 85, the figure of older men with cancer of the prostate will continue to increase. However, older adults' lifespan is determined by their prostate cancer and other concomitant medical conditions. This figure is so because PSA is a biomarker, and it is primarily high in the case of prostatic carcinoma, though this is incorrect because the increase level of PSA may be a biomarker for another disease (Catherine et al. 2004). Since there is an aggressive correlation between age and prostate cancer in several studies, this shows a higher figure in prostate cancer in older men than younger ones (Alicia et al. 2022). The main criterion for treatment is the likelihood of the patient living more than 10 years independent of chronologic age (Catherine et al. 2004), which concludes that the life expectancy of an older adult treated for prostate cancer is 10 years or longer.

6. Risk Factors for Prostate Cancer

Race, age, and a positive family history of prostate cancer are three proven risk factors for prostate cancer. Prostate cancer has also been linked to several other modifiable factors. However, the epidemiologic data regarding age, location, and a few observable factors concerning the beginning of prostatic carcinoma are summarized in the current review.

Frequent consumption of dairy products and meat are risk factors that may increase the likelihood of developing prostate cancer. Alcohol, in contrast, probably has little to no effect on the onset of prostate cancer. Also, nutritional supplements are less likely to save healthy men from developing prostate cancer Similarly, nutritional supplements are unlikely to save healthy men from developing prostate cancer. While smoking and being overweight have a limited correlation with prostatic carcinoma incidence, they have a favorable relationship with cancer of the prostate death. Other factors, such as eating fish, seem unrelated to prostate cancer incidents but have an inverse relationship with deadly prostate malignancy. Age seems to be very significant in the occurrence of prostatic carcinoma. According to the information from the United States monitoring, Epidemiology and End Results Program (Bethesda 2018) for the years 2000 to 2008, men between ages 40 and 44 have a 9.2/100,000 prevalence rate of prostatic carcinoma. Males within 70–74 years rapidly increased this rate to 984.8/100,000, followed by a minor drop (Bethesda 2018). Prostate cancer typically progresses at a slow pace, and dysplastic lesions may exist for years or even decades before the disease. According to extrapolations from autopsy studies, most men who lived to be over hundred years old would develop prostatic carcinoma (Gronberg 2003).

Bhanji et al. (2021) reviewed the genetic basis underlying hereditary predisposition to PCa, the current role of genetics and PCa risk assessment, and how genetic risk factors affect aggressiveness and lethality of PCa. The identification and characterization of alterations in prostate cancer (PCa)-predisposing genes can help to inform screening strategies in undiagnosed men and treatment options in men in both the clinically localized and in the metastatic setting. The number of prostate cancers discovered by chance at autopsies that were asymptomatic and not the cause of death implies that tiny, localized prostate cancers can go unnoticed for a long time before developing into clinically significant diseases (Bhanji et al. 2021).

Prostate cancer and physical activity and their correlation have been discussed in numerous epidemiologic researches, and these studies have found positive and negative relationships. A negative relationship between exercise and cancer of the prostate was shown in a recent meta-analysis of 24 case-control studies and 19 cohort researches released up to 2011 (Liu et al. 2011). When measuring the highest and lowest levels of overall physical activity, the combined data from the two research produced an RR of prevalent prostate malignancy of 0.90 (95%; CI=0.84-0.95). While the relationship between occupational and recreational exercise was insignificant (RR=0.95; 95%; CI=0.89-1.00), a somewhat more pronounced reduction in the incidence of prostatic carcinoma was seen with work activities (RR=0.81; 95%; CI=0.73-0.91). As a result, increase in exercise is linked to a little decline in the risk of cancer of the prostate overall and maybe a slight to a significant reduction in the chance of deadly prostatic carcinoma. By reducing persistent low-grade inflammation, a situation which has a clear correlation with prostate carcinogenesis, exercise may also reduce the prevalence of prostatic carcinoma (Sutcliffe et al. 2006; De Marzo et al. 2007). By reducing obesity associated with prostate cancer mortality, exercise may indirectly affect prostate cancer (Wright et al. 2007). Several case-control studies linked to a history of sexually transmitted diseases, particularly syphilis and gonorrhea, were linked to an elevated prostate malignancy risk (Dennis et al. 2002). However, the majority of these studies had a retrospective design, making them subject to bias. Latino males inhabiting in the United States of America in one

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recent prospective survey, (Cheng et al. 2010) who were once diagnosed of gonorrhea, had a high risk of prostatic carcinoma (RR=1.43; 95%; CI=1.07-1.91). However, Sutcliffe et al. (2006) cohort studies found a link between Trichomonas vaginalis infection and the chance of prostate malignancy, particularly in cases with advanced and lethal prostate cancer (Sutcliffe et al. 2006). In men *T. vaginalis* infection is frequently asymptomatic and, if left untreated, may result in chronic prostate inflammation. Though smoking has not traditionally been thought of as a prospect for cancer of the prostate, it has been estimated to be a causative agent in roughly thirty percent of all cancers globally (Sutcliffe et al. 2006).

7. Management/Treatment

The initial treatment for metastatic prostate cancer is androgen-deprivation therapy (ADT) through medical or surgical castration. In the past few years, results from several large, randomized, phase 3 clinical trials have shown longer survival, particularly among patients with high-risk or high-volume disease, when ADT was combined with either abiraterone acetate plus prednisone or docetaxel for metastatic prostate cancer at the time of initial ADT administration when the disease is castration sensitive (Sweeney et al. 2015; James et al. 2016; James et al. 2017; Fizazi et al. 2017; Feyerabend et al. 2018; Kassem et al. 2018; Kyriakopoulo et al. 2018). Apalutamide, an oral nonsteroidal antiandrogen agent that binds directly to the ligand-binding domain of the androgen receptor and prevents androgen-receptor translocation, DNA binding, and androgen receptor–mediated transcription, (Clegg 2012) has been approved in the United States and European Union for the treatment of patients with nonmetastatic, castration-resistant prostate cancer. The Targeted Investigational Treatment Analysis of Novel Anti-androgen (TITAN) trial was conducted to determine whether apalutamide would result in longer radiographic progression–free survival and overall survival than placebo with an acceptable safety profile and health-related quality of life among patients with metastatic, castration-sensitive prostate cancer who were receiving concomitant ADT (Chi et al. 2019). Nevertheless, a recent meta-analysis of 24 cohort studies found that heavy smokers had a statistically significant higher risk of prostate cancer (RR = 1.22; 95% CI = 1.01-1.46, highest versus lowest cigarettes/day) (Huncharek et al. 2010). Smoking is positively associated with prostate cancer mortality, as opposed to prostate cancer incidence, with smokers having a 14% higher risk of dying than nonsmokers (95% CI = 1.06-1.19). Through various mechanisms, including effects on sex steroid hormone levels, mutations in tumor suppressor genes like p53, and continued exposure to carcinogens like polycyclic aromatic hydrocarbons found in cigarette smoke, smoking may encourage the development of more aggressive, hormone-sensitive tumors (Zu and Giovannucci 2009).

7.1. The pharmacological approach

Since prostate cancer primarily affects elderly adults, there is a need for discussion and validation of the management of this disease. As life expectancy increases, the management of prostate malignancy will continue to be a significant concern in public health (Jean-pierre and Agnieska 2008). In other to discuss the pharmacological intervention of this disease, there is a need to discuss the treatment of prostate cancer.

***7.1.1. Hormone Therapy*:** The international guideline for the first intervention of hormone-sensitive metastatic prostatic carcinoma recommends androgen denial (Jean-pierre and Agnieska 2008); this intervention intends to inhibit the production of androgen/secretion in the testis and adrenal gland, to enable progress retardation, and avert probable catastrophic complications and effectually lessen symptoms and also the prostate tumor, thus averting prostate cancer growth but does not prolong survival (Ekaterina et al. 2018; Jean-pierre and Agnieska 2008). Care must be taken when administering androgen deprivation to the elderly, as careful monitoring for adverse events is advised. However, there is a link between castration and changes in body structure, which could be weight increase and fat mass, which implies decreased lean mass. These changes may also include cardiovascular mortality, elevated risk of diabetes, myocardial infarction, and elevated risk of severe osteoporosis (thought might have been present before castration). Osteoporosis leads to elevated risk of hip and other fractures, which have notable morbidity and death implications. Preventive and treatment strategy for osteoporosis, especially in the case of androgen denial and prostate malignancy, because males with hip fractures are likely to lose their lives within a range of 6 months. Thus, evaluation of the status of mineral bone mass, prevention of men engaging in long-term androgen denial, and treatment of osteoporosis with calcium and vitamin D prescriptions are all important. It is expedient to know that bisphosphonate therapy might be a better alternative for male patients with an elevated risk of fracture.

7.1.2. Chemotherapy: As it was stated in the hormone therapy procedure that androgen deprivation does not prolong survival; all males will eventually develop progressive diseases despite androgen being subdued and tumors becoming androgen-independent after a median of 18–24 months following medical or surgical castrations (Jean-pierre and Agnieska 2008). Several therapeutic medications are accepted for the treatment of prostatic carcinoma, via intravenous route, cabazitaxel and docetaxel are given every 3 weeks to avert tubulin depolymerization and,

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consequently, mitotic cell division occurs, which ultimately results in cell death. (Jean-pierre and Agnieska 2008). docetaxel has a common side effect known as Myelosuppression.

7.1.3. Immunotherapy: The cellular immunotherapy known as the recommended Sipuleucel-T. In this procedure, patients' peripheral blood mononuclear cells are prepared, and they are then cultured by leukapheresis in the sight of recombinant prostatic acid phosphatase (PAP) in combination with granulocyte-macrophage colony-stimulating factor to develop into antigen-presenting cells. To combat malignant prostate cells that exhibit high PAP levels, the activated product is then given back into the receiver over the course of three intravenous infusions. Because immunotherapy is expensive and requires numerous steps, the usage of sipuleucel-T is constrained (Jean-pierre and Agnieska 2008).

7.1.4. Targeted Alpha Therapy Approach: This targeted alpha therapy administered intravenously is called Radium-223 dichloride. It imitates calcium and selective is selectively taken up in the integral unit of the bone, osteoblastic bone metastases, and binds to hydroxyapatite (Ekaterina et al. 2018). In vivo experiments carried out in prostate cancer xenograft models reveal that once deposited in the new model intra-tumoral bone matrix, radium-223 dichloride has cytotoxic effects on adjacent tumor cells, osteoclasts, and disease-promoting osteoblasts by inducing irreversible DNA double-strand breaks, thereby disrupting positive feedback loops between tumor microenvironment cells and osteoblasts (Suominen et al. 2017). Radium-223 dichloride substantially improves comprehensive survival regardless of preceding docetaxel use while alleviating pain associated with bone metastases and with a favorable safety profile when given to castration-resistant prostate cancer (CRPC) patients (Nevedomskaya et al. 2018).

7.2. Non-pharmacological approach

While pharmacological and non-pharmacological treatment interventions are available, researchers recently assessed the results of some non-pharmacological management for prostate cancer using some non-pharmacological treatment for chronic prostate and pain in the pelvis by performing a comprehensive review of randomized controlled trials (Franco et al. 2018).

The researchers examined data that had been abstracted from 38 trials that included 3,290 males with CP/CPPS in 23 comparisons. The quality of the evidence was evaluated using the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) methodologies (QoE). Of these, Franco et al. (2018) found that the following non-pharmacological approaches, all based on short-term follow-up, may be practical:

7.2.1. Acupuncture (three studies, 204 participants) a good number of people experienced fewer prostatitis signs after receiving acupuncture as opposed to a placebo treatment. Comparing acupuncture to conventional medical therapy, the authors report that there may be minimal to no change in the adverse events and that it may help lessen the symptoms of prostate inflammation.

7.2.2. Circumcision (one study, 713 participants). Early circumcision probably decreases prostatitis signs slightly and might not be linked to an increased prevalence of adverse events compared with control, concluded the authors.

7.2.3. Lifestyle modifications (one study, 100 participants). Modification of lifestyle can also help with prostatitis improved signs in a good number of persons compared with the control.

7.2.4. Physical activity (one study, 85 participants). Compared with control, the ability to participate in exercise may have an effect in the decrease of prostate inflammation symptoms.

7.2.5. Extracorporeal shockwave therapy (three studies, 157 participants). When compared to a control, extracorporeal shockwave therapy lessens the symptoms of prostatitis. These findings might not hold true at a medium-term follow-up and might not be linked to a higher occurrence of negative outcomes.

7.2.6. Trans rectal thermotherapy likened to medical therapy (two studies, 237 participants). Compared to medical therapy alone, Trans rectal thermotherapy may slightly lessen the signs and symptoms of prostate inflammation. The authors stated that one study suggested that individuals might encounter brief detrimental effects.

7.3. Impact of age on treatment

An important factor in treatment decision-making, and in prostatic carcinoma, is age. Age affects the treatments doctors or oncologists suggest to patients. The present approach to treating prostate malignancy does not reflect recent research on older individuals' advantage from increasing treatment intervention (Hall et al. 2005). Survival by age Unlike some other cancers, age is less of a factor in survival rates for prostate cancer. This is partial because males are more diagnosed with prostate cancer after 70. Roughly six in 10 cases are diagnosed in men who are 65 years or older.

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8. Prognosis of Prostate Cancer

It is possible to cure and beat prostate cancer. The overall long-term survival rate increases when cancer is detected in stage 2 of the disease. For all prostate malignancies, the 5-year relative survival rate is 97.5%. In general, a man's chances of receiving effective treatment and continuing to be disease-free increase the sooner he is diagnosed with prostate cancer. Prostatic carcinoma has one of the best overall prognoses of all malignancies. The average five-year survival rate for prostate tumors found at the remote stage is just 28%, which is significantly lower than the rates for local and regional cancer of the prostate. Stage IV prostate cancers, when metastasized (spread) to lymph nodes, organs, or bones in other body parts, are represented by this average survival rate. The average long-term diagnosis for prostate cancer is relatively favorable because most cases are discovered by early screening procedures and are treatable. Improvements in therapy have enhanced survival times even for stage IV prostatic carcinoma and significantly decreased the number of deaths from cancer of the prostate.

Blood levels of PSA are frequently a reliable predictor of how well a treatment works or has been working. Although PSA readings are not always accurate, and occasionally doctors are unsure of what they signify, in general, PSA levels drop dramatically after treatment. Thus, it is essential to determine from the doctor what levels of PSA are normal before, during, and after treatment, as well as what levels would be cause for concern. Understanding that the PSA level is one aspect of the bigger picture is critical. If cancer is still present, if it is growing, or if it has returned, other causes may also be at play.

9. Prevention

There are not any definite measures to prevent prostate cancer. The danger can be reduced by following specific precautionary measures such as:

- Cut down on fatty foods
- Healthy diet rich in fruits and vegetables
- Have a daily exercise regimen
- Remain physically active
- Maintain a recommended weight
- Avoid smoking and alcohol

Early stages of prostatic adenocarcinoma do not cause symptoms, and no interventions for primary disease prevention have been established, although many methods are proposed to decrease risk. While a link between the incidence of more aggressive prostatic adenocarcinoma with smoking and obesity has been observed (Foerster et al.2018; Allott et al. 2013), the effect of lifestyle modifications, like cessation of smoking, increased exercise, and weight control, to decrease the danger of prostate cancer is not currently known. Instead, pharmacological agents, like 5α-reductase inhibitors (5-ARI), including dutasteride and finasteride, are proposed as chemo-preventative agents (Thompson et al. 2003). These agents function by preventing testosterone conversion to DHT, thereby reducing the activity of the AR; therefore, they could potentially prevent the development of prostate cancer, but clinical trials of their use had complex outcomes (Cuzick et al. 2014). The PCPT (Thompson et al. 2003) and REDUCE (Andriole et al. 2010)) study evaluated 5-ARI as chemoprevention in men with low PSA levels and no evidence of disease, finding that low tumors were less frequent. However, the incidence of higher-grade tumors was not affected. Thus, due to concerns over a lack of effect on high-grade tumor incidence, 5-ARIs have not been approved for prostate cancer prevention. However, results of the REDEEM study (Fleshner et al. 2012) showed an advantage of 5-ARI use as an adjunct to active surveillance, raising interest in their use in low-risk disease management. However, neither indication is usually recommended in any clinical guidelines (Cuzick et al. 2014).

10. CONCLUSION

The number of elderly patients with prostatic carcinoma will rise as long as life expectancy stays high, creating a significant therapeutic challenge for oncologists. Comprehensive geriatric evaluation and pertinent disease staging at diagnosis are necessary for properly managing these patients. This method will assist us in recommending the best course of action, focusing on maintaining the quality of life. Nevertheless, when the estimated survival probability is consistent with theorized indications for curative treatment, curative strategies should not be postponed.

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List of Abbreviation

PSA: prostate-specific antigen
QOL: quality of life
USPSTF: US Preventive Task Force
STDs: sexually transmitted infections
PAP: prostatic acid phosphatase
CRPC: castration-resistant prostate cancer
QoE: quality of evidence
GRADE: Grading of Recommendations Assessment, Development, and Evaluation
5-ARI: 5α-reductase inhibitors
RR: Relative risk
CI: Confidence interval
CP/CPPS: Chronic prostatitis/Chronic pelvic pain syndrome
PCPT: Prostate Cancer Prevention Trial
AR: Androgen receptor, DHT: Dihydrotestosterone
REDUCE: Reduction by Dutasteride of Prostate Cancer Events
REDEEM: Reduction by Dutasteride of clinical progression Events in Expectant Management

Authors' Contributions

Conceptualization: ETA, PNO, CPO, EOK. Project administration: ETA, PNO. Visualization: ETA, PNO, CPO, EOK. Writing-original draft: ETA, PNO, CPO, EOK. Review and editing: ETA, PNO, EOK.

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