REVIEW ARTICLE

The Burden and Management Of Castrate Resistant Prostate Cancer In Sub-saharan Africa: A Narrative Review

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ABSTRACT

Background: Castration-resistant prostate cancer (CRPC) represents a clinically significant stage of prostate cancer progression with a major therapeutic challenge, particularly in sub-Saharan Africa (SSA), where this disease burden is under-reported, and management is limited by access to novel therapies, financial constraints, and low research priorities.

This review discusses the epidemiology, underlying mechanisms and evolving therapeutic strategies for CRPC, with emphasis on accessibility and management challenges within SSA.

Methods: A narrative review was conducted using peer reviewed articles obtained from PubMed and Google Scholar, published over a 15-year period, using the Search terms; "castration-resistant prostate cancer", "non-metastatic CRPC", "metastatic CRPC", and "sub-Saharan Africa". Only English language studies and relevant international and regional guidelines were included.

Results: Prostate cancer is the most common malignancy and leading cause of cancer-related deaths among men in SSA, with an age-standardized incidence of 22.1 per 100,000, and mortality-to-incidence ratios that double those in high-income countries, having an age-standardized mortality rate of 8.4 per 100,000, which accounts for 12.3% of global deaths from prostate cancer. Hospital-based study reports a median overall survival of 11 months for CRPC in African population, however population-level data remains sparse, as most regional cancer registries do not capture disease progression.

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Conclusion: Modern therapeutic options have transformed the outcomes of CRPC globally, but equitable access in SSA remains limited. Strengthening regional cancer registries, fostering local clinical trials, and developing innovative financing strategies are essential to improve access and outcomes for men with CRPC in Africa.

INTRODUCTION

Prostate cancer is the commonest male malignancy in sub-Saharan Africa (SSA), with a disproportionately high mortality rate, compared on a global scale, and despite advances in therapeutic options of management, outcomes in SSA remain poor due to inequitable access to these novel therapies[1,2]. Castration-resistant prostate cancer (CRPC) represents a pivotal transition in disease progression where prognosis significantly worsens. There is limited data on the epidemiology of CRPC particularly in SSA, because many of the cancer registries across Africa do not capture the disease progression of prostate cancer to CRPC[3,4].

This review evaluates the epidemiology of CRPC, as well as its pathology, and management with a particular focus in SSA.

METHODOLOGY

This narrative review included peer-reviewed articles obtained from PubMed and Google Scholar (2010–2025), using the keywords: "castration-resistant prostate cancer", "non-metastatic CRPC", "metastatic CRPC", and "sub-Saharan Africa". Inclusion criteria included studies focusing on CRPC epidemiology, management, and outcomes within SSA. We also prioritized RCTs, meta-analyses, and international guidelines from the European Association of Urology, American Urological Association, and Society of Urologic Oncology (EAU 2024/25, AUA/SUO 2023). Non-English studies were excluded.

Epidemiological Burden of Prostate Cancer

Prostate cancer remains the second most frequently diagnosed cancer in men worldwide, and the most common in SSA. According to the Global Cancer Observatory (GLOBOCAN), there are about 1.47 million new cases and about 0.40 million deaths globally, with Africa showing a disproportionately high mortality-to-incidence ratio [1,2].

Prostate cancer is the leading cause of cancer and cancer-related deaths among men in SSA, with an Age Standardized Incidence of 22.1 per 100,000 population. Furthermore, the mortality-to-incidence ratios in SSA doubles those in high-income countries, with an Age Standardized Mortality Rate of 8.4 per 100,000, accounting for 12.3% of global deaths.[1,2]

While hospital-based study suggests a median overall survival of 11 months for CRPC, in-depth data on CRPC remains sparse across SSA, as cancer registries rarely capture this disease progression, highlighting the urgent need for improved surveillance. [3,4]

	Age Standardized Incidence Rate (per 100,00)	Age Standardized Mortality Rate (per 100,00)
Global Burden	29.4	7.3
SSA Burden	22.1 (5.9% of global new cases)	8.4 (12.3% of global deaths)

Table 1. Global vs SSA prostate cancer burden (GLOBOCAN 2022)

Pathobiology and Mechanisms of CRPC

Various mechanisms have been postulated to explain the occurrence of castrate resistant prostate cancer, such as; Androgen receptor (AR) amplification/mutations, which enables signaling at low androgen levels [5], and Intra-tumoral androgen synthesis, which allows for maintenance of local androgen supply [6.]

Other mechanisms involve the use of alternative signaling pathways by cancer cells, such as glucocorticoid receptor upregulation[7], as well as cellular epigenetic alterations such as DNA methylation and chromatin remodeling[8]. Furthermore, tumor microenvironment involving stromal/immune interactions, have been implicated in facilitating tumor growth [9].

These insights have driven the development of AR-targeted therapies and novel agents targeting DNA repair and radioligand pathways.

Diagnosis and Staging

According to the Prostate cancer Clinical Trial Working Group 3 (PCWG3), CRPC is defined as the progression of prostate cancer disease despite castrate testosterone levels (<50 ng/dL; <1.7 nmol/L) following Androgen Deprivation Therapy (ADT), with biochemical, radiological, or clinical progression[10]. It can either be non-metastatic or metastatic CRPC.

Non-metastatic CRPC (nmCRPC) is diagnosed when PSA rises without the presence radiographic metastasis. There are no detectable metastases on conventional or PSMA-PET imaging (Prostate Specific Membrane Antigen) [10].

Metastatic CRPC (mCRPC) on the other hand, involves disease progression on imaging or clinical symptoms despite ADT. PSMA-PET/CT has been found to be superior to conventional imaging in detecting micro metastatic disease and for staging, although its availability is limited in various parts of SSA, necessitating continued reliance on conventional bone scans and CT [11].

Treatment Modalities for CRPC

Following diagnosis of CRPC, all patients are continued on ADT, while specific treatment modality is based on the presence or absence of metastasis, associated symptoms, prior therapies, and patients' performance status and molecular profile.

Non-metastatic CRPC

Patient with high-risk nmCRPC, having a rapid PSA doubling time (PSADT) ≤10 months, would benefit from next-generation Androgen Receptor Inhibitors (ARIs) such as Apalutamide, enzalutamide, and darolutamide [12,13,14].

Apalutamide has been found to improve metastasis-free survival (MFS) in clinical trials (40.5 vs 16.2 months)[12], similarly, Enzalutamide also has Significant MFS benefit (36.6 vs 14.7 months) [13], and Darolutamide showed Improved MFS (40.4 vs 18.4 months) with favorable safety profile [14].

Metastatic CRPC

The therapeutic options for mCRPC include Androgen Receptor Signaling inhibitors (ARSIs) such as abiraterone which inhibits androgen synthesis, taxane-based chemotherapy such as docetaxel, radionuclide therapy, and PARP inhibitors (poly ADP-ribose polymerase enzyme inhibitors). Docetaxel with prednisone is the recommend standard first-line therapy for symptomatic mCRPC, while Cabazitaxel is also an effective alternative in patients with failed response to docetaxel and ARSIs [15].

The use of AR-targeted therapies such as Abiraterone with prednisone has been found to be associated with improved Overall Survival (OS), [16,17], similarly, with the use of Enzalutamide [18,19].

In the SSA context, the use of abiraterone, which is listed on the WHO essential medicines list, has been found to be the most feasible novel agent, however cost till remains a major challenge. Cost-saving interventions, such as the use of low dose-250 mg with food (off-label) shows similar Progression Free Survival (PFS), compared to the standard recommended fasting dose of 1000 mg dosing, and is given indefinitely as long as patient benefits from and tolerates the therapy[20].

Ketoconazole can be used as an alternative to abiraterone, which is also an inhibitor of testicular and androgen biosynthesis by inhibiting 17 alpha hydroxylases, however it also inhibits 11 alpha hydroxylase preventing synthesis of cortisol, hence low dose ketoconazole with replacement doses of hydrocortisone may be an effective therapy [21,22] Various forms of radiotherapies including the use of Radium-223 and 177Lu-PSMA has been found to prolong survival and palliate bone pain associated with metastatic disease[23,24,25]. Lutetium-177 (^{177}Lu)-PSMA-617 is a radioligand therapy that delivers beta-particle radiation to PSMA-expressing cells and the surrounding microenvironment[23]. PARP

inhibitors such as Olaparib and talazoparib with enzalutamide are particularly beneficial in patients with homologous recombination repair (HRR) mutations. [26,27]

Supportive and Palliative Care

Pain control should generally follow the WHO analgesic ladder. A Multidisciplinary care approach is essential in the management of CRPC, integrating oncology, urology, palliative medicine, and nursing care. Bone-targeted agents (such as Calcium/vitamin D, zoledronic acid, and denosumab) reduce skeletal-related events, while palliative radiotherapy provides effective pain relief. [28]

Treatment Algorithm within the SSA context

Given the resource limitation in SSA, and many other developing countries of the world, having a pragmatic approach in the management of CRPC within the SSA setting is justified, in order to address disparities in access and financial implications.

A recommended tiered approach towards the management of CRPC in SSA would include;

Tier-1: Continue ADT, commence docetaxel (if patient is fit), palliative radiotherapy (where available), bone protection therapy for bone metastasis (such as Calcium/vitamin D, zoledronic acid, and denosumab)

Tier-2: Continue ADT, commence abiraterone + prednisolone or enzalutamide, bone protection therapy for bone metastasis (such as Calcium/vitamin D, zoledronic acid, and denosumab), HRR testing (where feasible)

Tier-3: Incorporate darolutamide/apalutamide, cabazitaxel, PARP inhibitors, and 177Lu-PSMA radioligand therapy. (where available)

Limitations and Implementation Barriers in SSA

Limited drug access, high out-of-pocket costs due to low insurance coverage, and unavailable imaging infrastructure (PSMA PET/CT), pose significant challenge to the management of CRPC within the SSA context[1,2].

Furthermore, there is low research priority in SSA on CRPC, with sparce data on epidemiologic studies quantifying CRPC progression in SSA, as well as cost-effectiveness analyses of these novel medications within the African settings. There is hence the need for cancer registries that capture not just the disease burden of prostate cancer, but also the progression to CRPC. [3,4]

CONCLUSION

CRPC represents a clinically important subset of the global prostate cancer burden but remains poorly characterized in population-based statistics, especially in low-and-middle-income countries of SSA. Although modern therapies such as ARSIs, taxanes, PARP inhibitors and radioligand therapies, have extended survival and improved quality of life, limited access, high treatment costs and weak research infrastructure continue to constrain outcomes.

Improving access to affordable and appropriate evidence-based therapies, with the use of guideline-concordant care and resource-sensitive management algorithms are key priorities in these regions. There is also need for prospective, treatment-linked cancer registries that capture both the primary disease burden and progression to CRPC, alongside targeted epidemiological and cost effectiveness studies. These data will be essential for health-system planning, resource allocation and design of equitable access strategies aimed at improving survival outcomes for men with CRPC in SSA.

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