Real-world treatment patterns and clinical outcomes in patients with prostate cancer.

A single institution experience in Saudi Arabia

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ABSTRACT

Objectives: To describe the current real-world treatment landscape, sequence of therapies, and outcomes in patients with prostate cancer (PC).

Methods: A retrospective cohort study for PC patients diagnosed at King Abdullah Medical City Cancer Center in Makkah, Saudi Arabia, between January 2011 and December 2021. Data extracted from electronic medical records.

Results: A total of 282 patients with PC, with a mean age of 70 years and body mass index of 27. Among them, 274 (99%) had no family history of cancer, while 164 (58%) had hypertension and 125 (44%) had diabetes mellitus. Adenocarcinoma was the most common histology, found in 275 (97%) patients, with 99 (35%) having a Gleason score of 9. Notably, 184 (65%) patients presented with metastatic disease, and 147 (52%) with bone metastasis. While 198 (70%) patients underwent surgery, 184 (65%) did not receive radiotherapy. The most common first-line metastatic therapy was abiraterone in 23 (8%) patients, followed by enzalutamide in 7 (2.5%). During the study period, 167 (59%) patients survived, with an average treatment duration of 2.5 years.

Conclusion: This study provides insights into real-world treatment patterns and clinical outcomes in patients with PC. The findings of this study highlight the importance of adhering to treatment standards and making informed clinical decisions.

Keywords: prostate cancer, observational study, treatment patterns, therapy sequencing, next-generation hormonal agents

Saudi Med J 2024; Vol. 45 (6): 639-642
doi: 10.15537/smj.2024.45.6.20240042

Prostate cancer (PC) ranks among the most frequently diagnosed cancers in men worldwide, significantly impacting the global cancer burden, incidence, and mortality.[1] It is the most common malignancy in men, with over 174,000 new PC diagnoses and 31,000 related deaths estimated in the United States in 2019.[2] In Saudi Arabia, the prevalence of PC surpasses reported figures, and shows a steady increase in the incidence.[3]

Employing a multidisciplinary approach to address both localized and metastatic disease represents the best strategy for maximizing long-term survival. Watchful waiting and best supportive care are also viable options for selected cases.[4,5] Prostate cancer treatments may include surgery, radiotherapy, hormonal therapy, and chemotherapy, each carrying significant side effects, such as long-term urinary, psychosocial, cardiovascular, and sexual impairments. Therefore, oncologists need to carefully weigh the benefits and risks of each treatment, a decision-making process largely contingent upon well-informed patients.

Over the past decade, there have been substantial changes in PC management. However, real-world practice still lacks consensus regarding the optimal sequence or combination of these treatments.[2] Despite a few studies on PC in Saudi Arabia, evidence regarding the current treatment modalities and therapy sequencing in Saudi Arabia is scarce. Hence, to address this gap, we aimed to outline the current treatment landscape, therapy sequencing, and patient outcomes concerning PC in Saudi Arabia.

Methods. This was a single-institution retrospective, non-interventional cohort study that included patients diagnosed with PC at King Abdullah Medical City Cancer Center in Makkah, Saudi Arabia, between January 2011 and December 2021.

Structured data from electronic medical records, in addition to a manual review carried out by tumor registrars and experienced oncology staff, significantly improved the quality and effectiveness of the data extraction process. The collected variables at diagnosis comprised demographic (age, nationality, region of residence, and body mass index [BMI]), clinical (family history of cancer, presence of comorbidities, performance status, metastatic or non-metastatic disease, Gleason's score, and site of metastases), and

Disclosure. Authors have no conflict of interests, and the work was not supported or funded by any drug company.

treatment characteristics, which included surgical and radiation therapies, as well as first-, second-, third-, and fourth-line of treatments in metastatic PC. Outcomes related to metastatic cases such as death, survival, and length of stay during treatment were also collected.

We also collected information regarding androgen deprivation therapy (ADT) at initial diagnosis as ADT can be used in both non-metastatic PC. The treatment pattern analysis for metastatic PC involved evaluating the proportion of patients receiving first-, second-, and third-line life-prolonging therapies (abiraterone, bicalutamide, cyproterone acetate, docetaxel, enzalutamide, cabazitaxel, and apalutamide). Key information, such as duration of therapy and the date of death, was recorded in detail, specifying day, month, and year.

The study protocol was approved by the institutional review board of King Abdullah Medical City, Makkah, Saudi Arabia (IRB number: 22-965). The need for informed consent was waived off because we used de-identified data, and all procedures were carried out in accordance with the principles outlined in the Helsinki Declaration.

Statistical analysis. Electronic datasets provided by King Abdullah Medical City, Makkah, Saudi Arabia were analyzed using the Statistical Package for the Social Sciences statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). The analyses were subjected to stringent quality control processes, including verification of the Statistical Package for the Social Sciences programs and tests for data quality such as inaccuracies or missing data. All statistics were descriptive; for continuous variables, mean, standard deviation (SD), median, and minimum/maximum values were used to describe the data. Binary variables, such as metastatic status, were described in terms of the number of patients with the observed outcome relative to the total number of patients for whom the variable could be measured. The time-to-event study was the only one that included standard errors and confidence intervals (CIs).

Table 1 - Demographic and clinical characteristics.

Variables	n (%)
Age, median (min-max)	70 (35-94)
Nationality	
Saudi	203 (72.0)
Non-Saudi	79 (28.0)
BMI at initial diagnosis, median (min-max)	26.30 (14.20-44)
Presence of comorbidities	
Cardiovascular system	38 (13.5)
Hypertension	164 (58.2)
Diabetes mellitus	125 (44.3)
Performance status	
≤2	241 (85.5)
3	35 (12.4)
4	6 (2.1)
Metastatic	184 (65.2)
Non metastatic	98 (34.8)
Gleason score at initial diagnosis	
≤7	86 (30.5)
≥8	196 (69.5)
The metastatic site	
Bone	147 (52.1)
Visceral	12 (4.9)
Lymph node	22 (7.8)
None	99 (35.1)

Values are presented as numbers and percentages (%). min: minimum, max: maximum, BMI: body mass index

Results. Data were collected from a total of 282 patients. The patient demographics and clinical characteristics are presented in Table 1. The median age of patients in this study was 70 years and majority of the patients (72%) were Saudi. The median BMI of patients at initial diagnosis was 26.9.

With majority (98.9%) of them devoid of any family history of tumors. In addition, 96.8% patients did not have osteoporosis, 86.5% had no cardiovascular diseases, while 58.2% presented with hypertension and 44.3% presented with diabetes mellitus. Regarding performance status, 47.9% of the patients were assigned a grade of 2 and 36.5% received grade 1. Among those who underwent a prostate biopsy, 97.5% were diagnosed with adenocarcinoma. At diagnosis, 65.2% of patients were metastatic and 34.8% in the non-metastatic. Notably, at initial diagnosis, 7% patients had a Gleason score of less than 7, 23.4% patients scored 7, 25.5% patients scored 8, and 35% patients scored 9. More than half of the patients (52.1%) were diagnosed with bone metastases.

The treatment characteristics are reported in Table 2. Most of the patients, 70.2%, did not undergo surgery, and 65.2% did not receive radiotherapy. Notably, 8.2% received a combination of abiraterone, ADT, and bicalutamide as first-line, 2.5% received ADT and enzalutamide as second-line, and 5.3% received ADT and docetaxel for the third-line treatment.

According to the last contact with the patients, 59.2% were alive, while 40.8% had passed away. The median length of hospital stay after the treatment was 2.5 years (Table 3).

Discussion. On a global scale, the average age at the time of PC diagnosis is 66 years.[6] However, we found that the average age was slightly higher at 70 years,

Table 2 - Treatment characteristics.

Variables	n (%)
Surgery	
Radical retro pubic prostatectomy	15 (5.3)
Radical perineal prostatectomy	2 (0.7)
Transurethral resection of the prostate	40 (14.2)
Unmentioned	27 (9.6)
No surgery	198 (70.2)
Radiotherapy	
External beam radiotherapy	97 (34.4)
Brachytherapy	1 (0.4)
No radiotherapy	184 (65.2)
1st-line treatment	
ADT	176 (62.4)
ADT+bicalutamide	27 (9.6)
ADT+abiraterone	23 (8.2)
ADT+docetaxel	8 (2.8)
ADT+enzalutamide	7 (2.5)
ADT+cyproterone acetate	3 (1.1)
No treatment received	38 (13.5)
2nd-line treatment	
ADT+abiraterone	34 (12.1)
ADT+enzalutamide	33 (11.7)
ADT+bicalutamide	14 (5.0)
ADT+docetaxel	11 (3.9)
ADT alone	5 (1.8)
ADT+apalutamide	1 (0.4)
ADT+cabazitaxel	1(0.4)
No treatment received	143 (50.8)
3rd-line treatment	
No treatment received	186 (66.0)
ADT+abiraterone	20 (7.1)
ADT+enzalutamide	14 (5.0)
ADT+docetaxel	11 (3.9)
ADT alone	4 (1.4)

Values are presented as numbers and percentages (%).
ADT: androgen deprivation therapy

Table 3 - Outcome characteristics.

Variables	n (%)
Status of the last contact	
Alive	167 (59.2)
Dead	115 (40.8)
Length of stay in years, mean ± SD	2.52±1.99
Length of stay in years, median (min-max)	2 (0-10)

Values are presented as numbers and percentages (%).
SD: standard deviation, min: minimum, max: maximum

which may be attributed to delayed diagnosis and lack of screening programs for PC. Moreover, in our study, we found that men had an increased BMI, which is a factor known to increase PC risk, underscores the importance of targeted weight management initiatives, which can be implemented in the community to mitigate such risk.[7] Remarkably, we observed that only 1% of the patients had a family history of PC, which is significantly lower than the previously reported figures, which stood at approximately 10-15%. These findings emphasize the significance of personal risk awareness and family history in facilitating earlier diagnosis, timely treatment, and improved survival.

In our study, we observed that two-thirds of the patients displayed a Gleason score of 9, which indicates a poor prognosis, as highlighted by Nishimoto et al.[8] This aggressiveness can be partially explained by the higher BMI in our study population, which has been linked to an increased risk of aggressive PC.[9] Furthermore, our study demonstrated that nearly half of the patients had an Eastern Cooperative Oncology Group performance status of 2, a significant prognostic factor known to affect oncological outcomes such as survival, similar to previous studies.[10,11] This could be likely attributed to the presence of comorbidities, advanced age, and aggressive PC.

Our results highlighted the bone, lung, and liver as the most frequent sites of distant metastases, consistent with the findings of Bubendorf et al.[12] Although more than half of the patients had bone metastases, adedicated treatment plan tailored to this unique patient population becomes imperative.

Our study demonstrated that novel hormonal therapies (abiraterone and enzalutamide) were the predominant choices for first-line and second-line therapy, similar to a recently published data in the United States Medicare population.[13] Nevertheless, no significant differences in the treatment sequencing between novel hormonal therapies in clinical outcomes owing to cross-resistance between abiraterone and enzalutamide. Additionally, the use of chemotherapy (docetaxel or cabazitaxel) was relatively low, likely influenced by patient preferences, compromised performance, and frailty in this population. This highlights the pressing need to develop more effective treatment options for this population, both before and after chemotherapy.[2]

This study revealed that over the past 10 years, 60% of the overall patient population were alive during the study period, which is lower than the historic data published, which reported an 83% survival rate. The lower survival rate in our study can be attributed to the fact that one-third of patients were non metastatic, with an average treatment duration of 2.5 years.

This study seeks to address critical gap in knowledge and practice. The use of a robust data collection method is one of the strengths of this study. Moreover, the inclusion of all eligible patients reduced the risk of sampling errors.

Study limitations. First, the retrospective nature of the studies based on electronic health record could lead to some missing information on important variables. Second, the small sample size and single-center experience could impact the generalizability of the results, not all PC treatments were available at King Abdullah Medical City Cancer Center in Makkah, Saudi Arabia. Third, the study encompasses information on the overall population (early and metastatic PC), which could be more informatively analyzed when stratified by specific stages.

With the evolving landscape for PC treatment worldwide in early and metastatic disease, it is imperative to understand the current real-world treatment patterns and clinical outcomes among patients treated in Saudi Arabia to serve as a benchmark for future studies. We need to raise awareness within the community and among primary care physicians to emphasize early diagnosis and prevention of PC by weight management, appropriate screening, awareness of personal risk, and family history. Such measures are essential for avoiding complications and validating timely intervention while the disease is still manageable. Also, ensuring the availability and accessibility of novel treatments is vital for enhancing patients' quality of life and survival. In contrast, while the debate surrounding PC screening has persisted for decades, evidence suggests that it leads to a slight reduction in disease-specific mortality over 10 years but does not impact overall mortality. Hence, clinicians must carefully consider these benefits against the potential risks of screening, including the possibility of overdiagnosis and overtreatment, emphasizing the importance of shared decision-making based on patient understanding. Implementing these strategies, coupled with the dissemination of cancer prevention measures, can be expected to yield better quality of life, cancer-free survival, and improved overall survival.

In conclusin, given the challenging prognosis and aggressive nature of certain PC cases, there is an evident need for better strategies to ameliorate patient outcomes. Notably, novel hormonal treatments were the most common first- and second-line therapies. This highlights the importance of adhering to established treatment standards and informed clinical decision-making.

Acknowledgment. *The authors gratefully acknowldge Editage (www.editage.com) for the English language editing.*

Received 12th January 2024. Accepted 15th May 2024.

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