

Clinicopathological Features, Treatment and Outcome of Omani Patients with Metastatic Prostate Cancer

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Abstract

Objectives: Prostate cancer is the third most common cancer worldwide. The incidence is rising in the middle east. There is paucity of data about the clinicopathological features and outcomes of metastatic prostate cancer (mPCa) from the middle-east. We report the outcomes of mPCa from Oman.

Methods: Consecutive men diagnosed with mPCa and treated at the university hospital in Oman between January 2006 and December 2017 were included in this study. Information about demographics, clinical, laboratory, pathological and radiological features at presentation, treatment, and survival outcomes was collected. Data were gathered until April 2019 or until patient's death for progression-free survival (PFS) and overall survival (OS), whichever came first. Survival rates were estimated using the method of Kaplan and Meier. Univariate and multivariate analysis and Cox regression analyses were performed to study factors affecting the PFS and the OS.

Results: Out of the 239 men diagnosed with PC over the study period, 62 were diagnosed with mPCa. The median age was 71 (range 57 – 92) years. Majority of patients (61.3%) had a Gleason score ≥ 8 . Median PSA level was 100. Bone was the most common site of metastatic disease (90.3%). Majority of patients with hormone-sensitive disease were treated with testosterone suppression only, while abiraterone, enzalutamide and docetaxel were added for treating castrate resistant mPCa (mCRPC). After a median follow up of 34.5 months, the median PFS was 17 months, while the median OS was 43 months. Median survival post mCRPC was 17 months.

Conclusion: Omani patients with mPCa present with high PSA and Gleason score and with widespread metastatic disease burden. Treatments offered are according to internationally accepted standards and have comparable PFS and OS as reported elsewhere.

Keywords: Prostate Cancer, Metastatic, LH-Releasing Hormone, Abiraterone, Chemotherapy, Arabs, Oman

Introduction

An estimated 1.3 million men were diagnosed with prostate cancer (PCa) making it the 4th most common cancer in the world in 2018.¹ More than 350,000 men died of the PCa during the same year.¹ The incidence of PCa is lower in Arabs than compared to the western countries.² The lower incidence may be attributed, in part to lack of screening programs and the lower PSA levels due to smaller prostate gland size amongst Arabs.²⁻⁴ However, the incidence of PCa in Asian countries, including Oman, has been gradually increasing over the years. PCa was the 6th most common cancer in Oman in 2015.⁵⁻⁷ Incidence is less compared to Bahrain and Kuwait but higher than United Arab Emirates and Saudi Arabia.^{5, 8}

Medical or surgical castration remains the gold standard treatment for mPCa. For majority of men though, the disease escapes the lower testosterone levels and the cancer develops resistance to androgen deprivation, known as castrate resistant PCa (CRPC).^{9, 10} Docetaxel was the first agent to improve median overall survival (OS) and the quality of life (QoL) in mCRPC.⁹ Better understanding of the disease biology led to introduction of newer agents and various trials have now established the efficacy of agents blocking the androgen synthesis in improving the outcome of mCRPC. Together with docetaxel, these agents are now also used for the treatment of hormone sensitive mPCa (mHSPC).^{9, 10} Docetaxel, abiraterone and enzalutamide have been approved for the treatment of mHSPC while same agents along with radium-223, sipuleucel-T and cabazitaxel have been approved for the treatment of mCRPC.^{9, 10}

Differences in PCa incidence and associated mortality have been well recognised according to race and ethnicity despite living in same or different countries. These differences have been attributed to genetic and environmental factors as well as access to health care and screening programs.^{1, 4} Substantial data are available from different parts of the globe about survival rates of mHSPC or mCRPC, but there is scarcity of information from middle-eastern region.

Various studies from the region have reported the epidemiology of prostate cancer but limited data is available regarding the outcome of the PCa in Arabs.^{2, 3} We report the presenting features, treatment and outcome of men diagnosed with mPCa as well as factors affecting the survival in Omani men. To the best of our knowledge, this is the first of study reported from this region describing the survival outcomes for men with mPCa.

Methods

Consecutive patients diagnosed with mPCa at the Sultan Qaboos University Hospital (SQUH) between January 2006 and December 2017 were included in this study. SQUH is one of the 2 major hospitals in the country, situated in the capital city Muscat, providing cancer care to

patients from all over Oman. The majority of the patients were diagnosed and treated at SQUH. In case, the diagnosis was established elsewhere, tissue blocks were reviewed at SQUH.

Electronic patient records (EPR) were reviewed for demographic characters (age, co-morbid conditions and use of medicines for those conditions), clinicopathological features at presentation (PSA, Gleason score, clinical stage, organs involved, patient's performance status [PS]), the treatment received (first line and subsequent lines), and the survival till either the last date of follow up, or the date of death. Nadir PSA levels, as well as time to nadir PSA and time to PSA decline by 50% were also checked.

American Joint Committee on Cancer (AJCC) staging manual (8th edition) was used to stage the disease.¹⁰ Nadir PSA was the lowest PSA level documented on first line treatment for mPCa, while time to nadir PSA was the time from the start of the treatment to the time to reach nadir PSA level.¹¹ Patients with continuously rising PSA and testosterone levels below 1.7 nmol/L (0.50 ng/dL) were considered to have mCRPC.¹⁰ First line and subsequent treatment offered for mPCa were recorded. Patients diagnosed to have mPCa after or before the date of study period, not treated at SQUH or those who lost to follow up for more than 2 years or had incomplete data on EPR, and the patients with localized PCa were excluded from the analysis.

Kaplan-Meier method was used to estimate progression-free survival (PFS) and OS. PFS was defined as time period from the date of diagnosis of mPCa till disease progression. OS was defined as time from diagnosis to death or April 30, 2019, while OS2 was defined as the survival from the date of mCRPC to death or April 30, 2019. Chi-square test was for dichotomous variables while Log-rank test and Cox regression analysis were used for time to event. A p value of <0.05 was considered significant. The IBM Statistical Package for Social Sciences (version 20 for Windows; SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Institutional medical research ethics committee approval was sought.

Results

A total of 239 patients were diagnosed with PCa during the study period (January 2006 to December 2017). Out of those 62 had mPCa and met the inclusion criteria. This study reports on the presenting features and outcomes of these 62 patients.

Clinico-pathological features:

Median age was 71 (range 57 – 92) years. The vast majority of patients had at least one or more comorbidities (87.1%), hypertension being the most common (58.1%). Of all the patients, 25 (40.3%) were taking statin and 12 (19.4%) were on metformin for diabetes mellitus.

Trans-rectal ultrasound guided biopsy was the most common diagnostic method (61.3%). More than half of the patients (61.3%) had a Gleason score of ≥ 8 at diagnosis, and 56.8% had Gleason Score of 5 as primary or secondary pattern. Median PSA at the time of diagnosis was 100.00 ng/dL (range 3.0 – 4508.0), 50% of patients had PSA level of >100.00 at diagnosis. Staging studies revealed that 60 (96.8%) patients had had stage 4b disease. Bones were the most frequent site of metastases (90.3%), 40 (64.5%) patients had >10 lesions as seen on the bone scan, (table 1).

Table 1: Clinicopathological Features of all patients

Patient Characteristics	N (%)
Median Age	71 years
Comorbid Conditions	
None	8 (12.9)
Hypertension	36 (58.1)
Dyslipidaemia	22 (35.5)
Diabetes	19 (30.6)
Coronary Artery Disease	12 (19.4)
Statin Use	25 (40.3)
Metformin	12 (19.4)
Diagnostic Method	
TRUS*	38 (61.3)
TURP [‡]	15 (24.2)
Other Biopsy	7 (11.3)
PSA only	2 (3.2)
Gleason Score	
≤6	6 (9.7)
7	11 (17.7)
8	14 (22.6)
9	19 (30.6)
10	5 (8.1)
Missing	7 (11.3)
PSA Level	
<10	5 (8.1)
10 – 20	2 (3.2)
21 – 50	12 (19.4)
51 – 100	10 (16.1)
>100	31 (50.0)
Missing	2 (3.2)
Site of Metastasis	
Bone	56 (90.3)
Distant Lymph Nodes	19 (30.6)
Lungs	6 (9.7)
Liver	3 (4.8)
Number of Bone Metastases	
<4	10 (16.1)
4 – 10	6 (9.7)
>10	40 (71.4)
Missing	6 (9.7)

* TRUS = Transrectal Ultrasound Guided Biopsy

[‡] TURP = Trans Urethral Resection of the Prostate

Patterns of Treatment:

Of the 62 patients, 28 (45.1%) received androgen deprivation therapy (ADT, luteinizing hormone releasing hormone analogue or anti-testosterones alone), while 24 patients (38.7%) were treated with combined androgen blockade (CAB). Only 6 (9.7%) patients received upfront docetaxel along with the ADT. Median time to nadir PSA was 6 months (range 0 – 44), with median nadir PSA level of 0.55 ng/dL (range 0.01 to 1623). Median time to 50% drop in PSA was 2 months (range 2 - 39). A minimum testosterone level of 0.7 nmol/L was achieved in 79.0% patients. Minimum testosterone levels were achieved within 6 months in 25.8% patients (table 2).

Table 2: First line treatment offered to all patients

Patient Characteristics	N (%)
First Line Treatment	
ADT* only	27 (43.5)
Combined Androgen Blockade	24 (38.7)
ADT and Docetaxel	6 (9.7)
Surgical Castration only	2 (3.2)
Radical Prostatectomy and ADT	2 (3.2)
ADT and IMRT [†]	1 (1.6)
Time to Nadir PSA	
<6 months	30 (48.4)
>6 months	30 (48.4)
Missing	2 (3.2)
Minimum Testosterone Level	
<0.7	49 (79.0)
0.7 – 1.7	2 (3.2)
Missing	11 (17.7)
Time to minimum testosterone level	
<6 months	16 (25.8)
>6 months	35 (56.5)
Missing	11 (17.7)

* ADT = Androgen Deprivation Therapy

[†] IMRT = Intensity Modulated Radiation Therapy

The vast majority of patients (n = 40, 64.5%) developed mCRPC, slightly more than quarter of patients (n = 17, 27.4%) remained on their first line treatment, while in one patient neuroendocrine transformation was documented, whose disease continued to progress causing painful lymphadenopathy in groin with a PSA of 0.1 Biopsy of lymph node mass confirmed the diagnosis of neuroendocrine transformation of PC (table 3). PSA level was more than 20 ng/dL in 28 (68.2%) patients who developed mCRPC. Radiological progression was documented in 38 (92.7%) patients, while in the remaining 2 patients, a high PSA level with a low testosterone level was considered an indication of disease progression. Bone was the most common site of disease progression 29 (70.7%). At the time of confirmed mCRPC, 65.2% patients had a PS of 0 to 1. Most patients (n = 30, 75.0%) who developed mCRPC were treated with systemic cancer therapy. Abiraterone and docetaxel were the 2 most common agents used

(table 3). Of the patients treated with either docetaxel or abiraterone, one third of patients (n = 11, 36.66%) required dose reduction at some point during the treatment trajectory. PSA dropped by >50% in 13 (44.8%) patients within 3 months of starting the treatment. Disease progression was documented in 25 (86.2%) patients. Abiraterone was the most commonly used treatment option as the second line treatment for mCRPC, (table 3).

Table 3: Characteristics, Treatment Offered and Outcome of Patients with Progressive Prostate Cancer (n = 41)

Patient Characteristics	N (%)
Progressed to mCRPC*	40 (64.5)
Hormone Sensitive	17 (27.4)
Transformation to Neuroendocrine Tumor	1 (1.6)
Missing	4 (6.5)
PSA Level at mCRPC	
≤20	12 (29.2)
>20	28 (68.2)
Missing	1 (2.4)
Radiological Progression	
Yes	38 (92.7)
No	2 (4.8)
Missing	1 (2.4)
Site of radiological progression	
Bone Only	29 (70.7)
Lymph Nodes Only	3 (7.3)
Viscera and Lymph Nodes	3 (7.3)
Viscera Only	2 (4.8)
Bone and Lymph Node	1 (2.4)
Bone, Viscus and Lymph Node	1 (2.4)
Missing	2 (4.8)
Performance Status at mCRPC	
Performance Status 0	6 (14.6)
Performance Status 1	21 (51.2)
Performance Status 2	5 (12.1)
Performance Status 3	7 (17.0)
Performance Status 4	3 (7.3)
First Line Therapy for mCRPC	
Abiraterone with Prednisolone	12 (29.2)
Docetaxel ± Prednisolone	10 (24.4)
Enzalutamide	6 (14.6)
Best Supportive Care	9 (22.0)
Cabazitaxel [†]	1 (2.4)
Etoposide and Carboplatin	1 (2.4)
Patient Declined Therapy	1 (2.4)
Lost to follow-up	1 (2.4)
Adverse Events to Treatment	

None	16 (55.1%)
Fatigue	8 (27.6)
Neutropenia	2 (6.9)
Anemia	1 (3.4)
Volume Overload	1 (3.4)
PSA Response to Treatment	
PSA dropped by >50% in 3 months	13 (44.8)
PSA dropped by >50% in 6 months	15 (51.7)
PSA Increased	7 (24.1)
Disease Progression	
Radiological and PSA Progression	19 (65.5)
PSA Progression	5 (17.2)
Radiological Progression	1 (3.4)
Missing	4 (13.8)
2nd Line Treatment (n = 22)	
Abiraterone with Prednisolone	9 (40.9)
Docetaxel ± Prednisolone	3 (13.6)
Enzalutamide	3 (13.6)
Cabazitaxel	1 (4.5)
Irinotecan	1 (4.5)
Best Supportive Care	5 (22.7)
Bone Modifying Agents	
Zoledronic Acid	22 (53.6)
Denosumab	9 (21.9)
Zoledronic Acid followed by Denosumab	4 (9.7)
Alendronate	1 (2.4)
Skeletal Events	
Bone pain requiring radiotherapy	12 (29.2)
Bone pain requiring opiates	7 (17.0)
Bone fracture	1 (2.4)

* mCRPC = Metastatic Castrate Resistant Prostate Cancer

† Patient developed mCRPC soon after docetaxel

Bone modifying agents were used in 36 patients, zoledronic acid being the commonest agent (n = 22, 61.11%). Twenty (32.3%) patients had skeletal-related event, worsening bony pain requiring palliative radiotherapy being the commonest (n = 12, 60.0%), (table 3).

Progression free survival:

After a median follow up of 34.5 months (range 1 – 93), 4 (6.5%) are in complete remission, 16 (25.8%) were still receiving treatment, 20 (32.3%) died of disease progression; 13 (21.0%) died of a cause unrelated to disease or it's treatment, one (1.6%) died of treatment associated toxicity, one received best supportive care measures, while 7 patients (11.3%) did not return for follow up. Median PFS was 17.0 (range 4 – 91) months, (Figure 1). Age, bones metastases, number of bone metastases, time to nadir PSA, nadir PSA level, testosterone level of <0.7

nmol/L and type of first line treatment significantly affected the PFS on univariate analysis (table 4). None of the factors significantly affected PFS on multivariate analysis.

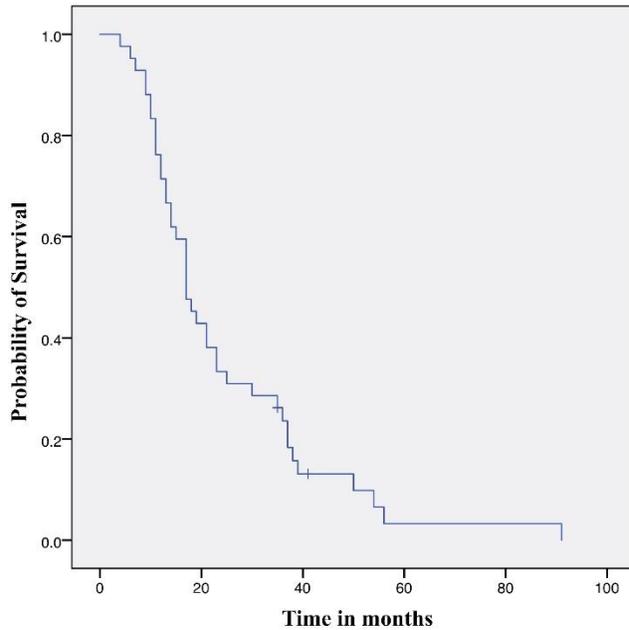


Figure 1: Progression free survival of all patients with metastatic prostate cancer at the time of diagnosis

Table 4: Univariate analysis for Progression Free Survival and Overall Survival 1 for all Patients with Metastatic Prostate Cancer (n = 62)*

Factor	Univariate Analysis for PFS				Univariate Analysis for OS			
	Median (months)	SE	CI 95%	p value	Median (months)	SE	CI 95%	p value
Diagnostic Method								
TRUS	19.0	2.6	13.8 – 24.1	0.04	53.0	7.1	39.0 – 67.0	<0.001
TURP	17.0	3.5	10.0 – 23.9		35.0	3.9	27.3 – 42.6	
PSA	10.0	-	-		1.0	-	-	
Other Biopsy	11.0	2.1	6.7 – 15.2		42.0	15.8	11.0 – 73.0	
Comorbidities								
None	11.0	0.5	9.9 – 12.0	0.17	13.0	3.5	6.0 – 20.0	0.002
One	17.0	13.8	0.0 – 44.1		64.0	17.2	30.1 – 97.8	
Two	19.0	2.8	13.3 – 24.6		47.0	5.8	35.5 – 58.4	
Three	18.0	4.4	9.2 – 26.7		42.0	8.7	25.0 – 59.0	
Statin Use								
Yes	18.0	2.0	14.0 – 21.9	0.24	Not Reached	-	-	0.007
No	14.0	2.5	9.1 – 18.8		40.0	4.2	31.7 – 48.2	
Gleason Score								
6	18.0	8.9	0.4 – 35.6	0.32	27.0	18.0	0.0 – 62.2	0.023
7	19.0	6.3	6.6 – 31.3		51.0	-	-	
8	21.0	5.2	10.7 – 31.2		Not Reached	-	-	
9	14.0	3.1	7.9 – 20.1		42.0	3.2	35.6 – 48.3	
10	11.0	1.6	7.8 – 14.2		35.0	14.0	7.6 – 62.3	
Liver Metastasis								
No	17.0	2.2	12.5 – 21.4	0.47	47.0	4.7	36.7 – 53.6	0.007
Yes	15.0	-	-		2.0	0.8	0.4 – 3.6	

Bone Mets								
Yes	17.0	1.21	14.6 – 19.3	0.04	42.0	2.9	36.2 - 47.7	0.1
No	39.0	11.6	16.1 – 61.8		Not Reached	-	-	
No. of Bone Mets								
<4	35.0	4.6	25.8 – 44.1	0.008	64.0	-	-	0.02
4 -10	38.0	26.2	0.0 – 89.5		64.0	-	-	
>10	15.0	1.5	12.0 – 18.0		38.0	7.1	24.0 – 52.0	
First Line Therapy								
ADT	19.0	4.5	10.1 – 27.8	0.014	-	-	-	-
CAB	17.0	1.4	14.2 – 19.7		-	-	-	
ADT + Docetaxel	14.0	8.1	0.0 – 30.0		-	-	-	
Time to nadir PSA								
<6 months	13.0	2.8	7.3 – 18.6	0.03	38.0	4.7	28.7 – 47.2	0.02
>6 months	25.0	13.4	0.0 – 51.2		64.0	12.0	40.4 – 87.6	
Minimum Testosterone Level								
<0.7 nmol/L	18.0	2.0	14.0 – 23.0	0.008	43.0	4.5	34.0 – 52.0	<0.001
0.7 – 1.7 nmol/L	10.0	-	-		12.0	-	-	
mCRPC								
Yes	-	-	-	-	42.0	2.2	37.6 – 46.3	0.003
No	-	-	-	-	Not Reached	-	-	
PSA at time of mCRPC								
<10	-	-	-	-	53.0	11.0	31.4 – 74.5	0.03
11-20	-	-	-	-	64.0	-	-	
>20	-	-	-	-	34.0	8.4	17.4 – 50.5	
Performance Status (PS) at time of mCRPC								
PS 0	-	-	-	-	Not Reached	-	-	0.005
PS 1	-	-	-	-	43.0	6.5	30.1 – 55.8	
PS 2	-	-	-	-	42.0	0.0	-	
PS 3	-	-	-	-	18.0	2.6	12.8 – 23.1	
PS 4	-	-	-	-	14.0	4.0	6.0 – 22.0	

* Continuous variables (e.g. age, PSA levels etc) not included, only categorical variables included in this table
ADT = Androgen Deprivation Therapy, CAB = Combined Androgen Blockade, CI = Confidence Interval, mCRPC = metastatic Castrate Resistant Prostate Cancer, OS = Overall Survival, PFS = Progression Free Survival, PSA = Prostate Specific Antigen, SE = Standard Error, TRUS = Trans Rectal Ultrasound Guided Biopsy, TURP = Trans Urethral Resection of Prostate

Overall survival I:

At a median follow up of 34.5 months (range 1 – 93), the median OS was 43 months (range 1 – 93, CI 95%, 33.5 – 52.5) (Figure 2A). Age, number of comorbidities, hypertension, statins use, Gleason score, number of bone metastases (Figure 2B), liver metastasis, PSA level at diagnosis, time to nadir PSA, nadir PSA level, testosterone level, (Figure 2C), complication with first line treatment, PFS, PSA levels at the time of mCRPC, visceral metastasis, PS at the time of disease progression, treatment duration for first line treatment for mCRPC, use of bone modifying agents and occurrence of skeletal-related event significantly affected the OS-1 on univariate analysis (table 4). None of the factors significantly affected PFS on multivariate analysis.

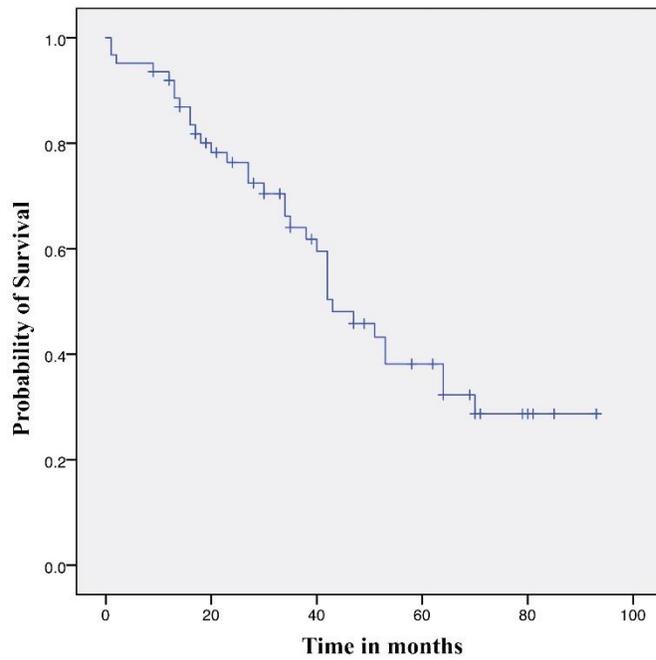


Figure 2A: Overall survival of all patients with metastatic prostate cancer at the time of diagnosis

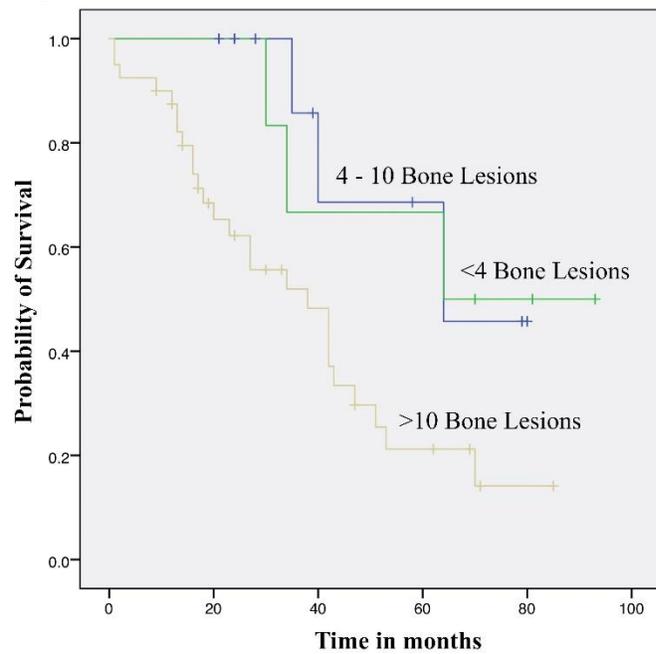


Figure 2B: Overall survival of all patients with metastatic prostate cancer at the time of diagnosis according to number of bone metastasis

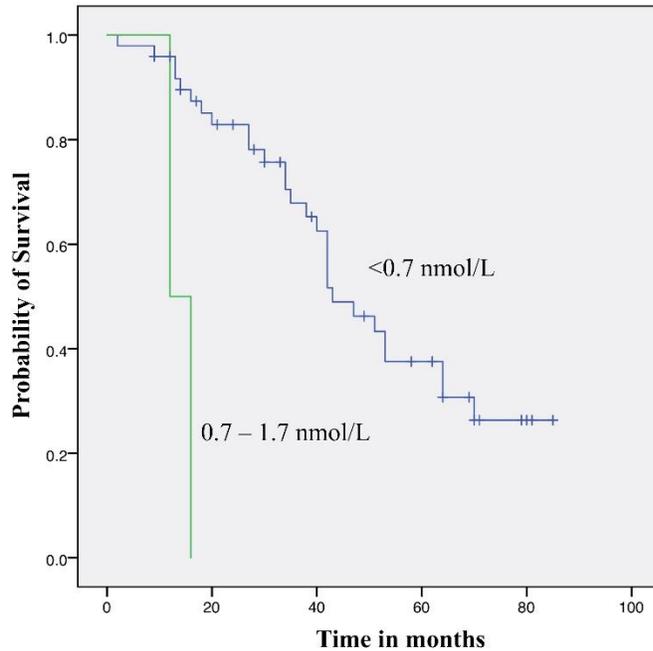


Figure 2C: Overall survival of all patients with metastatic prostate cancer at the time of diagnosis according to drop in testosterone levels

Overall survival 2 (OS post mCRPC):

The OS post mCRPC was 17 months (Figure 3A). On univariate analysis age, visceral metastasis, PS at the time of mCRPC, treatment for mCRPC, treatment dose reductions (Figure 3B), treatment duration of first line treatment for mCRPC, second line treatment for mCRPC and use of bone modifying agents significantly affected OS-2, while none of the factors were significant on multivariate analysis.

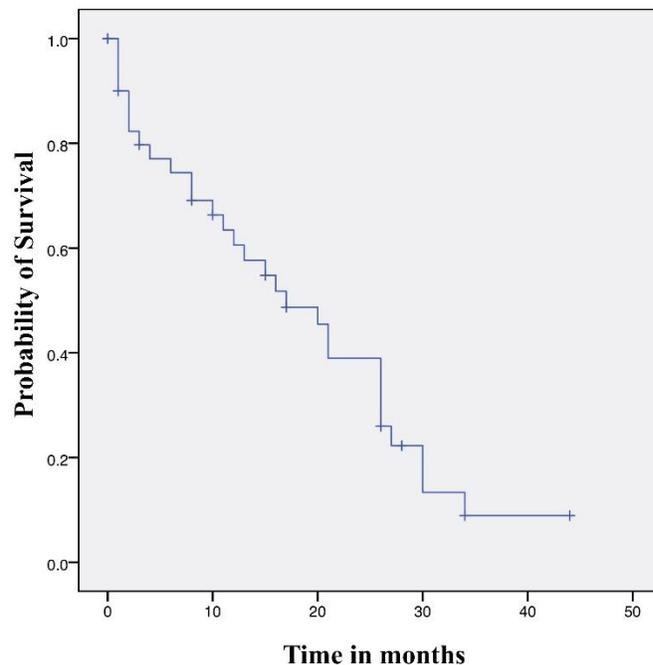


Figure 3A: Overall survival of patients with metastatic castrate resistant prostate cancer

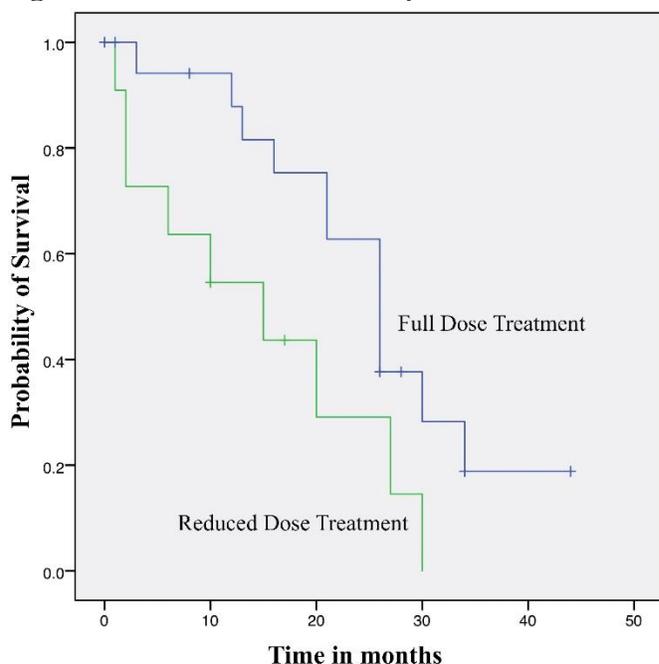


Figure 3B: Effect of Treatment dose reduction on Overall Survival of patients with metastatic castrate resistant prostate cancer

Discussion

Oman cancer registry captures the incidence of all cancers every year, but it does not collect data about the clinical stage, patterns of metastases, prognostic factors or outcome of cancer.⁵ For the first time we report the outcome of Omani men with mPCa. Majority of patients presented with poor risk features (high Gleason score and serum PSA level >20). Bone was the most common site of metastatic disease. The median PFS was 17 months, while the median OS was 43 months. Median survival post mCRPC was 17 months.

Increasing age is considered one of the risk factors for prostate cancer and age-specific incidence increases with each decade of life.⁸ Reported median age at the time of diagnosis ranges between 62 and 73 years across different continents. Median age of Asian men diagnosed with PCa is higher than European Americans or African-Americans.¹² Median age at diagnosis in our cohort was 71 years. Our results are consistent with those reported from Europe, Asia and from Sub-Saharan Africa.^{3, 11, 13, 14}

Asian men with PCa have higher serum PSA levels, a higher Gleason score and a higher clinical stage at diagnosis compared to European or American patients. Serum PSA in Asian men is also reported to be higher than African men living in America or Africa.¹² Studies from India, Egypt, Hong Kong, Japan and Nigeria also support these findings.^{3, 11, 14-16} Our results are consistent with these studies, as the median PSA level was 100.0 ng/mL. Similarly 61.3% patients had a Gleason scores of 8 or above. The combination of PSA levels and Gleason scores were significantly higher compared to the studies reported from India, Nigeria and Egypt.^{3, 14, 15}

Median time to nadir PSA and nadir PSA levels have significant impact on the survival outcomes of PCa.^{11, 16} Median nadir PSA level was 0.55 ng/mL with a median time of 6 months to nadir PSA in our cohort. The results are consistent with studies reported from Japan and Hong Kong, which revealed a median time to nadir PSA of 6 - 7.3 months.^{11, 16} All these studies found nadir PSA levels and median time to nadir PSA significantly affecting the PFS and OS.^{11, 16} A study from Nigeria,¹⁴ reported a nadir PSA of 4 ng/mL with a PFS and OS of 26.8 and 40.3 months respectively. Although the median nadir PSA level was much higher in this study in comparison to our results (4.0 vs. 0.55 ng/mL), median PFS was longer in Nigerian men as compared to our patients (26.8 vs. 17.0 months), however, OS was almost identical (40.3 vs. 43 months). All these studies indicate the difference in PCa outcomes in different patient populations with various median nadir PSA levels.

The overwhelming majority of patients had bone metastases at the time of disease diagnosis with nearly two thirds of patients having >10 bony lesions. Almost similar figures were reported from Egypt, India and Hong Kong,^{3, 15, 16} though number of patients and extent of bony lesions were lesser than our cohort.

Interest to treat the primary PCa even in presence of metastatic disease increased after encouraging results from other diseases e.g. breast, colon and ovarian cancer.¹⁷ At least 2 randomized trials (HORRAD and STAMPEDE) and a meta-analysis showed beneficial effect of radiotherapy to the primary site and improved OS by 7% at 3 years for patients with low metastatic disease burden (defined as <5 bone metastases and no visceral disease).¹⁰ STAMPEDE trial also showed improved PFS, failure free survival and prostate specific survival in favour of localized radiotherapy, when added to the standard ADT. NCCN and European Society of Medical Oncology (ESMO) have incorporated the option of using radiotherapy with ADT for treating the primary site in patients with mHSPC with low disease burden.^{10, 18} Besides radiotherapy to the primary tumour, radical surgery to the primary site also improves the 5-year OS and disease-specific survival.¹⁷ In our cohort, only one patient was treated with ADT and radiotherapy while 2 had radical surgery at the time of diagnosis because of low metastatic burden. Both HORRAD and STAMPEDE were reported in 2019 and 2018 respectively while the cohort of patients described here includes patients from 2006 onwards which can make it easier for a reader to understand the low number of cases.

Medical castration with either ADT or CAB or surgical castration was the standard of care before the approval of docetaxel and newer hormonal agents for mPCa.¹⁹ In the last decade, treatment for PCa has taken significant strides. PFS and OS have increased significantly for patients with mHSPC with the addition of docetaxel and abiraterone earlier in the disease course.^{9, 10} Risk of death reduced by 24% (STAMPEDE trial) to 27% (CHAARTED trial) with docetaxel while by 37% (STAMPEDE trial) to 38% (LATITUDE trial) with abiraterone.^{9, 10} The vast majority of patients in our cohort were treated with either single agent ADT or CAB. Only 6 (9.7%) patients received upfront docetaxel along with ADT. Upfront docetaxel or abiraterone were approved for mHSPC or high risk prostate cancer after 2018 while we report our cohort since 2006, hence it is easy to understand few patients being treated with upfront docetaxel in our report. We cannot compare our results to results reported from Egypt as all patients were treated with upfront docetaxel for mHSPC in that study.³ Due to small numbers

treated with upfront docetaxel and shorter follow up it was too early to see the effect on PFS or OS.

Median PFS of mHSPC or time to the development of mCRPC is reported to be 18 – 24 months.^{9,20} Median time to CRPC was 17 months in our cohort which is better than reported from India¹⁵ and Hong Kong,¹⁶ while considerably lower than that reported from Nigeria.¹⁴ Age, PSA level and number of bony metastasis were significant factors affecting the time to mCRPC in our as well as the study reported from India,¹⁵ while median nadir PSA levels and median time to nadir PSA were significant factors as reported from Hong Kong and Nigeria.^{14,16} Treatment with docetaxel, abiraterone and enzalutamide has improved the survival of patients with mCRPC.¹⁰ All three agents were used for our cohort once patients developed mCRPC (28 of 40 patients). It should be noted, that whereas, the median OS for mCRPC used to be 10 – 12 months prior to docetaxel and the hormonal agents,²⁰ there has been a significant improvement with the introduction of these agents, and our results of median OS (OS 2) of 17 months is consistent with the published literature.⁹

Median OS for studied cohort was 43 months which is shorter than reported from India¹⁵ but better than reported from Hong Kong.¹⁶ Various factors (patient PS, Gleason score, visceral metastases, PSA, haemoglobin, lactate dehydrogenase (LDH), albumin and alkaline phosphatase at the time of diagnosis) were tested for predicting the outcome of patients with mCRPC treated with various agents enrolled on 6 different clinical trials in various settings.²¹ The prognostic score could predict 4 groups with worst median survival of 8.8 months and longest survival of 22.8 months.²¹ Likewise another group suggested a simpler prognostic score comprising of PSA, LDH, neutrophil to lymphocyte ratio, and patient's PS for a relatively small sample size of patients treated with abiraterone.²² On an univariate analysis, Gleason Score, PSA levels and PS significantly affected the OS in our cohort.

There are several limitations of our study. The sample size was small and the cohort was treated over a long time period, during which treatment options for mPCa have changed considerably. Although we report outcome of Omani men with mPCa from a single centre, but this still can be a representative sample for the country to a large extent as only 2 hospitals in the Sultanate provides cancer care and receive referrals from all over the country.

Conclusion

In conclusion, Omani men with mPCa present with high PSA levels, a higher cumulative Gleason score and a high risk disease. The OS was comparable to reported outcome from various regions of the world.

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Geographical information: Oman

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