Evaluating the Prognostic and Therapeutic Significance of PSA in Prostate Cancer

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ABSTRACT

Prostate cancer (PCa) remains one of the most prevalent malignancies in men and a leading cause of cancer-related mortality worldwide. Despite diagnostic advances, disparities in outcomes persist, particularly in resource-limited settings. This study aimed to evaluate the prognostic utility of prostate-specific antigen (PSA) dynamics and key clinical parameters, including complications and Gleason score, in predicting disease progression and mortality among PCa patients in Oman. A retrospective cohort study was conducted at a tertiary care center in Sohar hospital, Oman, involving 20 histologically confirmed PCa patients treated between 2019 and 2024. Data collected included baseline and follow-up PSA levels, Gleason scores, TNM staging, treatment modalities, treatment-related complications, and survival outcomes. Patients were stratified by disease progression and survival status. PSA levels during follow-up, presence of complications, and disease progression were significantly associated with mortality. In the multivariate Cox model, complications (HR = 0.091, 95% CI: 0.010–0.821, p = 0.033), follow-up PSA levels (HR = 0.988, 95% CI: 0.977–0.999, p = 0.039), and disease progression (HR = 0.089, 95% CI: 0.009–0.900, p = 0.040) emerged as independent predictors of decreased survival. Gleason scores were significantly higher among deceased patients, though not significant after adjustment. Unexpectedly, younger age was associated with increased mortality risk. Follow-up PSA levels, complication status, and disease progression provide clinically relevant prognostic information in prostate cancer patients. These findings support the use of dynamic PSA monitoring and individualized follow-up strategies to improve clinical decision-making, particularly in resource-constrained settings.

Keywords: prostate specific antigen; prostate cancer; survival analysis; gleason score; cox proportional hazards model

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INTRODUCTION

Prostate cancer (PCa) is the most frequently diagnosed malignancy among men worldwide and represents a major global health concern. In 2020, over 1.4 million new cases were reported, and the number is projected to rise to 2.9 million by 2040 due to aging populations and increasing life expectancy[1]. Although many cases are low-risk and asymptomatic at diagnosis, advanced disease can cause significant morbidity, including painful skeletal metastases, spinal cord compression, anemia, and renal complications from obstructive uropathy[2]. In recent decades, the diagnostic landscape of PCa has evolved significantly. Prostate-specific antigen (PSA) testing remains central to early detection, with new approaches integrating early-life PSA levels, single nucleotide polymorphisms (SNPs), and biomarker panels to refine risk stratification. Multiparametric magnetic resonance imaging (MRI) has improved the detection of clinically significant PCa, allowing more targeted biopsy and treatment decisions[3]. However, these advancements also introduce challenges related to overdiagnosis and overtreatment, particularly for indolent cancers that may never progress[4].

Despite global progress, disparities in screening and diagnosis persist. In the Middle East, and particularly in Oman, prostate cancer detection typically occurs at later stages due to the absence of formal screening programs and limited public awareness[5]. According to regional studies, Oman has one of the lowest age-standardized incidence rates of PCa. However, the age-standardized mortality rate was reported at 4.5 per 100,000 in 2021—suggesting delayed diagnoses and more aggressive presentations[6,7]. Without national PSA screening guidelines, early detection remains underutilized, and the burden of advanced disease disproportionately affects healthcare resources.

PSA is not only a screening marker but also a valuable tool for prognosis and disease monitoring. Persistent PSA levels (>0.1ng/mL) after radical prostatectomy are strongly associated with higher risks of biochemical recurrence, disease progression, and cancer-specific mortality[8]. In high-risk patients undergoing radiotherapy with androgen deprivation therapy (ADT), post-treatment PSA levels above 0.1ng/mL similarly indicate poorer outcomes[9]. In metastatic hormone-sensitive PCa, early PSA kinetics—including a ≥90% decline within 12 weeks—are predictive of improved progression-free survival[10]. Emerging biomarkers such as the Prostate Health Index (PHI), which integrates (-2)proPSA, free PSA, and total PSA, offer improved discrimination between aggressive and indolent cancers, potentially reducing unnecessary biopsies[11,12].

PSA also plays a key role in therapeutic monitoring. In metastatic castration-resistant PCa (mCRPC), combining PSA with circulating tumor DNA (ctDNA) tumor fraction enhances prognostication. Detectable ctDNA at early treatment cycles is associated with shorter overall survival, irrespective of PSA trends[13]. Despite strong international evidence, region-specific data on the prognostic and monitoring utility of PSA in PCa are limited in Oman.

In this context, we conducted a retrospective study at a tertiary care center in Al Batinah North, Oman, to evaluate the prognostic and therapeutic utility of prostate-specific antigen (PSA) in patients with prostate cancer. By analyzing baseline PSA levels and longitudinal PSA kinetics throughout treatment, this study aims to assess their correlation with disease severity, recurrence, and survival outcomes. Given the limited access to advanced diagnostics in resource-constrained settings, our findings may offer preliminary insights to guide clinical decision-making and highlight the potential for more effective use of PSA as a cost-efficient biomarker. While sample size limitations restrict definitive conclusions, this study provides a foundation for understanding prostate cancer outcomes in the Omani context and identifies priorities for future research in the region.

MATERIALS AND METHODS

Study Design and Setting: This study was a retrospective cohort analysis conducted at a tertiary care centre in Sohar hospital, Oman, to assess the clinical characteristics and outcomes of patients diagnosed with PC. Medical records spanning a period of 5 to 10 years were systematically reviewed. All data were anonymized before analysis, and the study was approved by the institutional ethics committee of the hospital.

Study Population: Patients were eligible for inclusion if they had a histologically confirmed diagnosis of prostate cancer, documented PSA levels at diagnosis and during follow-up, and complete information regarding treatment modality whether surgery, radiation, or hormone therapy as well as outcome data including disease progression and survival. Patients were excluded if their medical records were incomplete, if follow-up data were insufficient, or if they had other malignancies known to affect PSA levels. A total of 255 patients were initially screened for inclusion, of whom 61 were excluded due to incomplete records or loss to follow-up. However, based on hospital records from 2019 to 2024, only 20 patients with confirmed prostate cancer and available PSA data were identified and included in the final analysis (Figure 1).

Variable Definitions: The variables extracted and analyzed in this study included prostate-specific antigen (PSA) levels, disease progression, survival outcomes, treatment response, comorbidities, family history, and ethnicity. PSA levels were measured in ng/mL and categorized into three risk groups: low risk (<10 ng/mL), intermediate risk (10–20 ng/mL), and high risk (>20 ng/mL)[14]. Disease progression was defined as a rise in PSA during or after treatment, radiologic evidence of metastasis, or the initiation of second-line therapy[15]. Survival outcomes were evaluated using progression-free survival (PFS), defined as the time from diagnosis to clinical or biochemical progression, and overall survival (OS), defined as the time from diagnosis to death or last follow-up[16]. Treatment response was classified as complete response, partial response, stable disease, or disease progression[17]. Comorbidities such as diabetes, cardiovascular disease, hypertension, and chronic kidney disease were identified from physician notes or ICD-10 codes. Family history was recorded based on the presence of prostate cancer in first-degree relatives. Ethnicity was categorized as Omani, South Asian, or other.

Sample Size Estimation: Sample size was calculated using Cochran's formula for finite populations. Assuming a PCa prevalence of 10.1% in Oman, a minimum of 140 patients was required (95% confidence

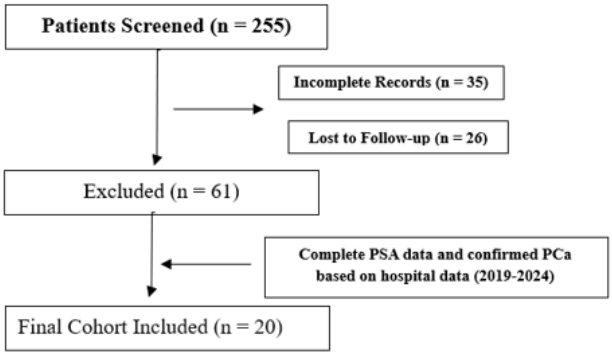

Figure 1. Flowchart of Patient Selection

level, 5% margin of error). To compensate for incomplete data, a 20% inflation factor was applied, yielding a target of 168 patients, which was exceeded in the final cohort. However, despite the initial sample size projection, only 20 eligible prostate cancer patients with complete PSA data and follow-up information were available from hospital records between 2019 and 2024. This limitation reflects the practical challenges of data availability in our institutional setting and is acknowledged as a significant constraint of the study.

Data Collection and Quality Control: Data were extracted from the hospital's electronic medical records system (Al-Shifa) using structured query terms. The extracted data included demographic information such as age, ethnicity, and family history; clinical variables including comorbidities, PSA levels, and treatment modality; and outcome measures such as disease progression, recurrence, metastasis, and survival. To ensure accuracy, data quality control was performed through double-entry validation and cross-checking by two independent researchers. Patients with missing PSA values or incomplete survival data were excluded from the analysis.

Statistical Analysis: All statistical analyses were conducted using SPSS software (version 27). Continuous variables were expressed as mean ± standard deviation, while categorical variables were reported as counts and percentages. The association between PSA levels and disease severity was assessed using correlation analysis. Kaplan-Meier survival curves were generated to estimate OS and PFS. To identify predictors of survival outcomes, multivariable Cox proportional hazards models were constructed, adjusting for age, PSA level, comorbidities, and treatment modality. Missing data were handled using complete case analysis, and no imputation was performed. A two-tailed p-value of less than 0.05 was considered statistically significant.

Ethical Considerations: The study was approved by the Institutional Ethics Committee of College of Medicine and Health Sciences, National University of Science and Technology, Sohar, Oman (approval number: NU/COMHS/EBC0011/2025 dated 06/02/2025) and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. The requirement for informed consent was waived by the Ethics Committee due to the retrospective nature of the study and the use of anonymized, de-identified patient data.

RESULTS

Baseline Characteristics Stratified by Disease Progression and Survival Status

A total of 20 prostate cancer patients were included in the analysis, with stratification into groups based on disease progression (n = 18) and survival status (n = 20). Among the 18 patients analyzed for disease progression, 10 were classified as stable (no progression), while 8 experienced disease progression. For survival status, 13 patients were alive at last follow-up and 7 were deceased. Baseline characteristics between groups are summarized in Table 1.

No statistically significant differences were found in age or PSA levels at diagnosis across disease progression or survival groups ($p > 0.05$). However, the distribution of Gleason scores showed a significant difference between survivors and deceased patients ($p = 0.015$), indicating a higher score in the deceased group. Additionally, Gleason score showed a borderline association with disease progression ($p = 0.060$), while TNM staging and treatment modality did not differ significantly across progression or survival groups ($p > 0.05$). Recurrence rates were low (11.1%) and showed no statistically significant differences across either stratification group.

Similarly, complications were significantly more prevalent among those with disease progression (87.5% vs. 30.0%; $p = 0.015$). The follow-up duration was significantly longer in deceased patients compared to those alive (3.40 vs. 0.56 months; $p = 0.027$), suggesting a potential link between extended follow-up and mortality (Table 1). Further analyses, revealed that the mean Gleason score was significantly higher in the deceased group (8.33 ± 0.52) compared to those alive (7.08 ± 1.00), confirmed via both t-test ($p = 0.011$) and Mann–Whitney U test ($p = 0.015$) (Table 2). However, baseline and follow-up PSA values did not significantly differ between disease progression groups or survival groups ($p > 0.05$), despite higher mean values in the progression and deceased subgroups (Table 3 and Table 4).

Association Between Clinical Covariates and Mortality Risk

A multivariate Cox proportional hazards model was constructed to assess predictors of survival (Table 5). Among the tested variables, age, complications, PSA follow-up, and disease progression showed significant associations with survival status ($p < 0.05$). An unexpected finding was the inverse relationship between age and mortality, where older patients demonstrated lower risk of death ($\beta = -0.141$, HR=0.868, 95% CI: 0.771-0.978, p=0.020). Given the small sample size and potential for type I error, this finding is most likely a statistical artifact rather than a true biological relationship. The limited number of events (n=7 deaths among 20 patients) may have resulted in unstable parameter estimates and chance findings. On the other hand, treatment complications were strongly predictive of mortality ($\beta = -2.402$, HR = 0.091, 95% CI: 0.010–0.821, $p = 0.033$), indicating markedly increased risk of death in patients who experienced complications. Similarly, PSA levels during follow-up were also significantly associated with survival ($\beta = –0.012$, HR = 0.988, 95% CI: 0.977–0.999, $p = 0.039$), with lower PSA values linked to improved prognosis. Patients with disease progression had significantly higher mortality risk compared to those with stable disease ($\beta = –2.415$, HR = 0.089, 95% CI: 0.009–0.900, $p = 0.040$). Although treatment modality showed a high hazard ratio (HR=17.888), the effect was not statistically significant (p=0.092), and the extremely wide confidence interval (95% CI: 0.622-514.367) reflects substantial uncertainty and suggests overfitting. This estimate should not be interpreted clinically and highlights the limitations of multivariate modeling in small cohorts. Other covariates, including PSA at diagnosis ($p = 0.908$) and Gleason score ($p = 0.629$), did not significantly influence mortality in the adjusted model.

Survival Analysis and Prognostic Implications

Kaplan-Meier survival analysis revealed a counterintuitive finding where the estimated mean survival time was 3.29 years (SE=0.522; 95% CI: 2.263-4.308) for deceased patients and 2.11 years (SE=0.351; 95% CI: 1.422-2.800) for survivors. This apparent paradox is a methodological artifact resulting from differential censoring patterns. Deceased patients were followed until death (complete observation), whereas surviving patients were censored at their last documented follow-up, which often occurred early in their disease trajectory. This does not imply that deceased patients lived longer, but rather reflects longer observation time before event occurrence versus early censoring in survivors. The log-rank test (Mantel-Cox) approached but did not reach statistical significance (χ^2=3.666, p=0.056), indicating that survival curves did not significantly diverge within the observation period (Table 6). The survival function (Figure 2) and hazard function (Figure 3) further illustrate the divergence in outcomes based on follow-up and survival status. Collectively, these findings underscore the clinical importance of PSA follow-up values and complications as predictive markers in managing prostate cancer patients.

Table 1. Baseline Characteristics Stratified by Disease Progression and Survival Status

Characteristic	Disease Progression				Survival Status			
	Overall (n = 18)	**Stable (No) (n = 10)**	**Progression (Yes) (n=8)**	**Test Statistic**	**Overall (n = 20)**	**Alive (n = 13)**	**Deceased (n = 7)**	**Test Statistic**
Age (years), Median (IQR)	–	76.50 (5)	68.00 (19)	21.00 (0.091)	–	74.50 (12)	76.00 (28)	41.00 (0.721)
PSA at Diagnosis (ng/mL), Median (IQR)	–	2.12 (82.05)	18.61 (103.75)	23.50 (0.142)	–	0.93 (47.14)	8.09 (107.23)	30.50 (0.331)
Gleason Score (mode)	3+3 (3), 3+4 (1), 4+3 (2), 4+4 (7), 4+5 (2), 5+4 (1)	3+3 (3), 3+4 (1), 4+3 (1), 4+4 (2), 4+5 (1)	4+4 (5), 4+3 (1), 4+5 (2)	15.00 (0.060)	3+3 (4), 3+4 (2), 4+3 (2), 4+4 (7), 4+5 (2), 5+4 (1)	3+3 (4), 3+4 (2), 4+3 (2), 4+4 (3), 5+4 (1)	4+4 (4), 4+5 (2)	**11.00 (0.015)** **
TNM Stage (mode)	T3b–T4, N1, M0/M1 (1); M1b (1); T4, N1, M1 (1); N1M1 (1)	–	T3b–T4, N1, M0/M1 (1); M1b (1); T4, N1, M1 (1); N1M1 (1)	–	T3b–T4, N1, M0/M1 (1); M1b (1); T4, N1, M1 (1); N1M1 (1)	T3b–T4, N1, M0/M1 (1); M1b (1); N1M1 (1)	T4, N1, M1 (1)	4.00 (0.261)
Primary Treatment Modality (n)	Hormone therapy (16), Radiation (1), Combination (1)	Hormone therapy (8), Radiation (1), Combination (1)	Hormone therapy (8)	1.80 (0.407)	Hormone therapy (17), Radiation (2), Hormone Therapy / Radiation (1)	Hormone therapy (11), Radiation (1), Hormone Therapy / Radiation (1)	Hormone therapy (6), Radiation (1)	0.74 (0.692)
Complications, n (%)	Yes: 10 (55.6%) No: 8 (44.4%)	Yes: 3 (30.0%) No: 7 (70.0%)	Yes: 7 (87.5%) No: 1 (12.5%)	**5.95 (0.015)** **	Yes: 11 (55.0%) No: 9 (45.0%)	Yes: 8 (61.54%) No: 5 (38.46%)	Yes: 3 (42.86%) No: 4 (57.14%)	0.64 (0.423)
Recurrence, n (%)	Yes: 2 (11.1%) No: 16 (88.9%)	Yes: 1 (10.0%) No: 9 (90.0%)	Yes: 1 (12.5%) No: 7 (87.5%)	0.03 (0.867)	Yes: 2 (11.1%) No: 16 (88.9%)	Yes: 1 (9.10%) No: 10 (90.90%)	Yes: 1 (14.29%) No: 6 (85.71%)	0.12 (0.732)
Mortality, n (%)	–	3 (30.0%)	4 (50.0%)	–	–	–	–	–
Follow-up (months), Median (IQR)	–	0.68 (5.28)	2.02 (121.85)	19.00 (0.519)	–	0.56 (2.31)	3.40 (256.38)	7.00 (0.027) **

Test Variable: Age (Continuous), PSA Diagnosis (Continuous), Gleason Score (Continuous), TNM Stage (Category - T3b-T4,N1,M0 or M1 as 1, M1b as 2, T4,N1,M1 as 3 & N1M1 as 4), Treatment Modality (Category – Radiation as 1, Hormone Therapy as 2 & Hormone Therapy / Radiation as 3), Complications (Category – No as 0 & Yes as 1), Recurrence (Category – No as 0 & Yes as 1), Mortality (Deceased), PSA Followup (Continuous). Grouping Variable: Disease Progression (1 – Stable (No) & 0 – Progression (Yes)), Survival Status (1 – Deceased, 0 – Alive); Test Statistic is Mann-Whitney U test for Continuous Variable and Chi-Square test for Category Variable. Values in the parentheses denotes the significant value ** $p<0.05$.

Table 2. Independent samples tests for Gleason Score by Survival Status

	Survival Status	**n**	**Mean ± SD**	**t-test**	**p-value**	**Mann-Whitney U Test**	**p-value**
Gleason Score	Alive	12	7.08 ± 1.00	-2.857	0.011	11.00	0.015
	Deceased	6	8.33 ± 0.52				

Survival Status: Alive:0, Deceased:1; ** $p<0.05$

Table 3. Independent samples tests for PSA Diagnosis and PSA Follow up by Disease Progression

	Disease Progression	**n**	**Mean ± SD**	**t-test**	**p-value**	**Mann-Whitney U Test**	**p-value**
PSA Diagnosis	Stable (No)	10	65.64 ± 162.36	0.551	0.589	23.500	0.142
	Progression (Yes)	8	103.74 ± 121.38				
PSA Follow up	Stable (No)	8	13.79 ± 34.95	1.004	0.335	19.000	0.519
	Progression (Yes)	6	73.98 ± 166.95				

Disease Progression: Progression (Yes):0, Stable (No):1

Table 4. Independent sample tests for PSA Diagnosis and PSA follow-up by Survival Status

	Survival Status	n	Mean Rank	Mann-Whitney U test	p-value
PSA Follow up	Alive	10	6.20	7.00	0.027**
	Deceased	5	11.60		
	Total	15			

TestVariable: PSA Follow up; GroupingVariable**:** Survival Status (1 – Deceased, 0 – Alive);** p<0.05.

Table 5. Cox Proportional Hazard Model

Covariates	Beta	SE	p-value	HR	95.0% CI for HR	
					Lower	Upper
Age	-0.141	0.061	**0.020****	0.868	0.771	0.978
PSA Diagnosis	0.002	0.014	0.908	1.002	0.974	1.030
Gleason Score	0.265	0.549	0.629	1.303	0.445	3.821
Treatment Modality	2.884	1.714	0.092	17.888	0.622	514.367
Complications	-2.402	1.125	**0.033****	0.091	0.010	0.821
PSA Follow up	-0.012	0.006	**0.039****	0.988	0.977	0.999
Disease Progression	-2.415	1.178	**0.040****	0.089	0.009	0.900

Dependent Variable: Survival Status (1 – Deceased, 0 – Alive); HR – Hazard Ratio, SE – Standard Error, CI – Confidence Interval, ** p<0.05, Covariates: Age (Continuous), PSA Diagnosis (Continuous), Gleason Score (Continuous), Treatment Modality (Category – Radiation as 1, Hormone Therapy as 2 & Hormone Therapy / Radiation as 3), Complications (Category – No as 0 & Yes as 1), PSA Followup (Continuous) and Disease Progression (Category – Progression (Yes) as 0 & Stable (No) as 1).

Table 6. Kaplan Meier Test

Survival Status	Mean[a]				Log-Rank (Mantel-Cox)
	Estimate	Std. Error	95% Confidence Interval		
			Lower Bound	Upper Bound	
Alive	2.111	0.351	1.422	2.800	
Deceased	3.286	0.522	2.263	4.308	3.666 (0.056)
Overall	2.625	0.328	1.983	3.267	

a. Estimation is limited to the largest survival time if it is censored. Values in the parentheses denotes the significant value. Disease Progression: Progression (Yes):0, Stable (No):1; Time: Follow-up Duration (<1 year as 1, 1-3 years as 2, 3-5 years as 3, 5-10 years as 4 &>10 years as 5); Status: Disease Progression; Factor: Survival Status (1 – Deceased, 0 – Alive)

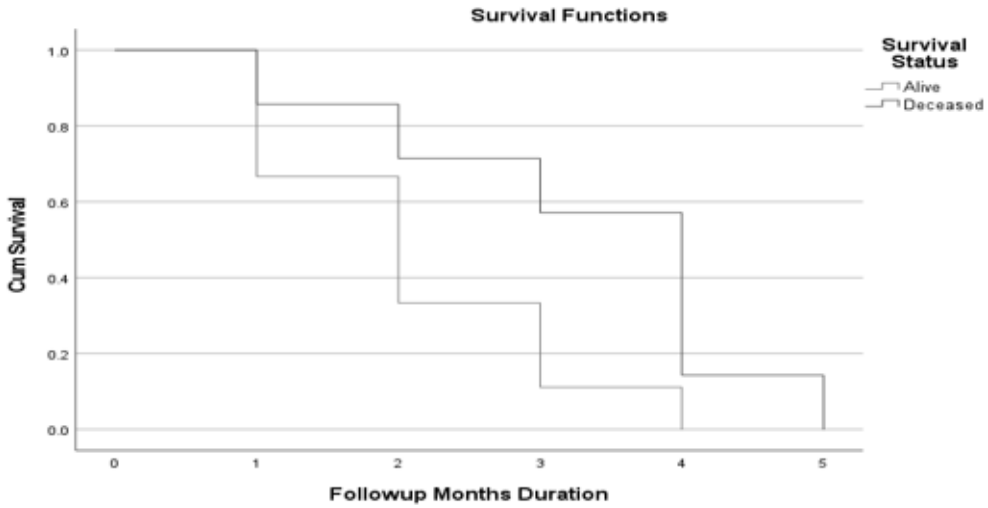

Figure 2. Survival Function showing Kaplan-Meier estimates stratified by survival status. Note: The counterintuitive survival pattern reflects differential censoring and immature data rather than actual survival advantage in deceased patients.

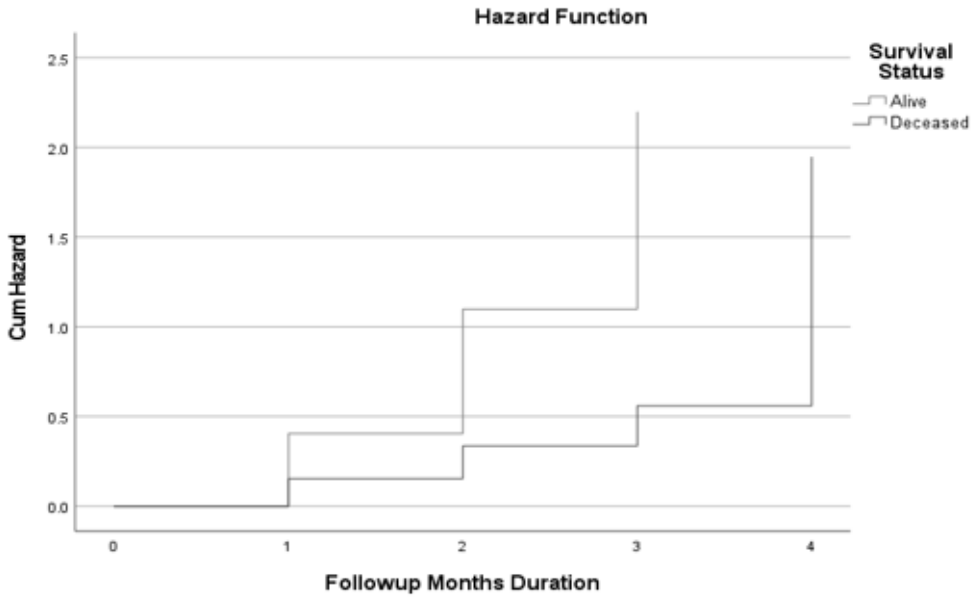

Figure 3. Hazard Function showing Kaplan-Meier hazard estimates stratified by survival status.
Note: The hazard pattern demonstrates the instantaneous risk of event occurrence over time, with the counterintuitive pattern similarly reflecting differential censoring and immature data rather than actual hazard differences between groups

DISCUSSION

This study investigated clinical predictors of disease progression and mortality in prostate cancer patients, with a focus on PSA dynamics, treatment-related complications, and key clinical variables such as age and Gleason score. Despite the limitations of a small sample size (n = 20), the analysis revealed several statistically and clinically relevant patterns consistent with emerging literature supporting the value of post-treatment PSA monitoring and complication status as key indicators of poor outcomes. Recent reviews have underscored that longitudinal PSA trends may outperform baseline levels in predicting recurrence and survival in treated prostate cancer patients[18].

Consistent with recent research, PSA levels at diagnosis were not predictive of mortality, whereas elevated PSA levels during follow-up were significantly associated with worse survival outcomes. This supports growing evidence that post-treatment PSA kinetics—including doubling time, nadir PSA, and PSA velocity—provide greater prognostic utility than baseline PSA levels alone[18–22]. Although this study did not directly assess PSA slope or doubling time, the independent association between higher follow-up PSA and mortality underscores the value of dynamic PSA monitoring in post-treatment surveillance[21,22].

Gleason score, long established as a strong predictor of disease aggressiveness and survival, was significantly higher among deceased patients in univariate analysis. However, it did not remain significant in the multivariate model. This attenuation may reflect collinearity with follow-up PSA or disease progression status—both of which can mediate the clinical effects of histologic grade. Similar findings have been reported in multivariable models where dynamic or composite markers outperformed static histopathological features[19]. Alternatively, the limited sample size may have restricted statistical power, masking the Gleason score's independent contribution. Nonetheless, the observed association in unadjusted comparisons reinforces its continued relevance in risk stratification.

An unexpected finding was the inverse relationship between age and mortality. Older patients demonstrated a lower risk of death, which contrasts with most studies where advancing age correlates with poorer outcomes. However, this paradox is supported by some recent reports suggesting that early-onset prostate cancer may be biologically more aggressive or subject to overtreatment-related toxicity[23]. Additionally, selection or referral bias in this small, homogeneous cohort may have contributed to this result. Further research is needed to clarify whether younger patients inherently have more aggressive disease or are disproportionately impacted by treatment-related morbidity.

Another notable observation involved treatment complications. While complications were significantly more common among patients with stable disease, they were independently associated with increased mortality in the adjusted Cox model (HR = 0.091, p = 0.033). This apparent contradiction may be explained by treatment intensity bias: patients with better-controlled disease may have undergone more aggressive or prolonged therapies, increasing their exposure to complications. Alternatively, the presence of complications may indicate underlying systemic vulnerability, inflammatory responses, or subclinical progression not captured through routine imaging or biochemical monitoring. Previous studies have similarly reported that complications may portend worse outcomes, not solely due to treatment side effects but also as proxies for frailty or aggressive disease biology[24]. These findings highlight the need for careful monitoring and complication mitigation, especially in patients receiving intensive multimodal therapy.

Disease progression was strongly associated with mortality. Patients with progression had significantly worse survival compared to those with stable disease (β = –2.415, HR = 0.089, p = 0.040). Although the reference group in our coding was patients with disease progression, the result clearly demonstrates that disease stability confers a substantial survival advantage. This is consistent with data from Shore et al.[25], who reported that radiologic progression following curative treatment was the strongest predictor of mortality in non-metastatic prostate cancer. It reinforces the clinical importance of longitudinal disease monitoring to detect subtle signs of progression early.

Finally, Kaplan-Meier analysis revealed a counterintuitive result: immature survival data due to short and incomplete follow-up. The

paradoxical survival estimates and near-significant log-rank test (p=0.056) suggest that survival curves may diverge meaningfully with extended observation time. However, at the current stage of data maturity, definitive conclusions about survival differences cannot be drawn. This underscores the need for prospective studies with longer, complete follow-up to accurately characterize survival outcomes in this population."

Limitations

This study has several important limitations. The critically small sample size (n=20) compared to the calculated requirement (n=168) represents the most significant constraint. With only 20 patients and seven covariates in the multivariate Cox model, the analysis is susceptible to overfitting, where the model may describe random noise rather than true biological relationships. This is evidenced by the extremely wide confidence interval for treatment modality (HR=17.888; 95% CI: 0.622-514.367), which renders this particular estimate statistically unreliable and clinically uninterpretable. The small sample size also limits statistical power to detect true associations and increases the risk of Type II errors. Furthermore, parameter estimates may be unstable, and the generalizability of findings to broader populations is substantially limited. As a retrospective, single-center analysis, the study is vulnerable to selection bias and residual confounding. The absence of molecular or genomic data restricts biological interpretation, particularly in understanding how PSA kinetics and complications may reflect tumor behavior. Additionally, the homogeneous cohort limits the broader applicability of findings across diverse demographic or clinical subgroups. The paradoxical age finding, where older patients demonstrated lower risk of death (HR=0.868, 95% CI: 0.771-0.978, p=0.020), is most likely a statistical artifact given the small sample size and potential for type I error. The Kaplan-Meier survival paradox, where deceased patients showed longer mean survival times, reflects data immaturity and methodological artifact rather than clinical reality. Given the small sample size, these results should be considered exploratory and hypothesis-generating, requiring validation in larger, prospective cohorts. Despite these constraints, the study provides preliminary data from an underrepresented region and demonstrates alignment of PSA kinetics findings with established international literature. These findings underscore the need for individualized follow-up strategies and support the integration of dynamic biomarkers into routine clinical decision-making, while highlighting the necessity for future prospective, multicenter studies with adequate sample sizes, standardized PSA kinetics assessment, and molecular stratification to validate these associations and overcome current statistical limitations.

CONCLUSION AND RECOMMENDATIONS

In summary, this study identifies several key clinical variables—specifically follow-up PSA levels, disease progression, age, and complications—as significant predictors of survival in prostate cancer patients. Although Gleason score and baseline PSA were not independently predictive in the multivariate model, their associations in unadjusted analyses remain consistent with established evidence. The paradoxical patterns observed with age and complications highlight the complexity of cancer outcomes and the influence of treatment-related and biological confounders. These findings support a more dynamic, individualized approach to post-treatment surveillance. Future prospective, multicentre studies with adequate sample sizes, standardized PSA kinetics assessment, and molecular stratification are essential to validate these associations, overcome current statistical limitations, and develop robust risk stratification tools for prostate cancer care in resource-constrained settings. To overcome the limitations inherent in single-center studies from resource-constrained settings, multi-institutional collaborations within the Gulf Cooperation Council (GCC) region should be prioritized. Pooling data from multiple centers in Oman, United Arab Emirates, Saudi Arabia, Kuwait, Bahrain, and Qatar could achieve adequate statistical power while maintaining regional relevance. Standardized data collection protocols, shared electronic health record systems, and coordinated follow-up mechanisms would enable robust studies that provide actionable insights for the region.

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