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Prognostic Significance of High-Risk versus Very High-Risk Classification in Non-Surgically Managed Prostate Cancer: A Retrospective Cohort Study

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Background: Risk stratification is one of the most critical parameters guiding treatment decisions in nonmetastatic prostate cancer. Although it is well established that high risk (HR) and very high risk (VHR) groups diverge prognostically, the real-world impact of this distinction in non-surgically managed patient populations has been less extensively evaluated.

Methods: In this retrospective study, 81 patients with nonmetastatic prostate cancer were analyzed (HR: n=24; VHR: n=57). All patients received androgen deprivation therapy (ADT), and 65.4% additionally underwent radiotherapy (RT). Clinical and pathological characteristics, early PSA responses, overall survival (OS), and disease-free survival (DFS) were compared between HR and VHR groups.

Results: At diagnosis, VHR patients presented with higher PSA values, worse Gleason scores, and more advanced stages. Although PSA responses at three and six months were similar between groups, long-term outcomes were significantly inferior in the VHR cohort. Median OS for the entire cohort was 72.1 months in VHR patients versus 97.1 months in HR patients (p=0.039). Among those receiving RT, the difference was preserved (HR: 104.5 months vs VHR: 75.1 months; p=0.032). Median DFS was 23.3 months in the VHR group and 44.5 months in the HR group (p=0.026). During follow-up, recurrence/metastasis occurred in 54.4% of VHR patients compared with 16.7% of HR patients (p=0.002).

Conclusion: Our findings show that the VHR classification maintains strong prognostic value even in non-surgically managed patients, underscoring its role as a biologically distinct and aggressive disease entity. Standard RT+ADT seems insufficient in this subgroup. The study supports exploring intensified treatment strategies, such as prolonged ADT, brachytherapy boost, pelvic nodal RT, and, where appropriate, novel androgen receptor signaling inhibitors or chemotherapy.

Keywords: prostate cancer, high risk, very high risk, radiotherapy, androgen deprivation therapy, survival

Introduction

Prostate cancer is one of the most common malignancies among men and remains a leading cause of cancer-related mortality worldwide with significant geographical variations in incidence and mortality.[1,2] The clinical course is highly heterogeneous; while low-risk and indolent cases may remain stable for long periods, high -risk (HR) and very high -risk (VHR) subgroups are prone to rapid progression and markedly increase the risk of mortality.[3] Accurate risk stratification therefore plays a central role in predicting the natural history of the disease and in selecting appropriate treatment strategies.[4]

Several risk classification systems are used to guide prognosis and therapy, including the National Comprehensive Cancer Network (NCCN),[5] the European Association of Urology (EAU),[6] and the Cambridge Prognostic Groups (CPG), the latter offering a 5-stage model with potentially superior discriminatory power for predicting cancer-specific mortality.[7,8] Among these, the NCCN's HR and VHR categories have gained particular importance in clinical decision-making over the past decade. VHR classification is based on criteria such as the presence of a predominant Gleason pattern 5, extensive positive biopsy cores in Grade Group 4–5 tumors, or locally advanced T3b–T4 stage disease, reflecting the coexistence of multiple adverse factors.[9] As shown in the landmark study by Sundi et al (2014), VHR

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classification is linked with a threefold higher risk of metastasis and a sevenfold higher risk of prostate cancer-specific mortality.[10] These findings firmly established VHR disease as a biologically distinct and aggressive clinical entity.[10]

Standard treatment approaches for high-risk localized prostate cancer typically consist of radical prostatectomy or definitive radiotherapy combined with long-term androgen deprivation therapy (ADT).[11] However, outcomes in the VHR population remain unsatisfactory, with long - term survival rates failing to reach acceptable levels.[12] Furthermore, the treatment landscape is rapidly evolving with the integration of novel systemic agents (eg, abiraterone, enzalutamide)[13,14] and advanced diagnostic tools (eg, PSMA-PET),[15] while research into biomarkers, including microRNAs and the gut microbiome, is expanding our understanding of disease biology and prognosis.[16–18] Despite these advances, evidence directly examining the prognostic impact of VHR classification in non-surgically treated patients receiving ADT ± RT is relatively limited, despite the fact that many real-world patients are managed this way due to surgical unsuitability, comorbidities, age/frailty, or patient preference.[19,20]

The present study retrospectively analyzed a cohort of nonmetastatic HR and VHR prostate cancer patients who did not undergo surgery. The aim was to compare baseline clinical characteristics, early treatment responses, OS and DFS between HR and VHR subgroups, and to interpret these results against contemporary literature in order to clarify the prognostic significance of VHR classification in non-surgically treated populations.

Materials and Methods

Study Design and Patient Population

This retrospective cohort study was conducted at the Department of Medical Oncology of Van Training and Research Hospital. The study included a total of 81 patients who were diagnosed with nonmetastatic high - risk (HR) or very high - risk (VHR) prostate cancer and treated with androgen deprivation therapy (ADT) with or without radiotherapy (RT) between January 2015 and December 2022. Risk classification was defined according to the National Comprehensive Cancer Network (NCCN) guidelines.[5]

Inclusion and Exclusion Criteria

Patients were eligible if they had histologically confirmed prostate adenocarcinoma and met the HR or VHR criteria at diagnosis. Only patients without evidence of distant metastasis (M0) at baseline imaging were included. Exclusion criteria were as follows: a history of another malignancy, prior radical prostatectomy or systemic chemotherapy, incomplete medical records or death within the first 30 days after treatment initiation. Patients with active infection, severe uncontrolled systemic disease or insufficient follow -up information were also excluded. Reasons for non-surgical management were documented and included patient preference, comorbidities (eg, cardiovascular disease, frailty), advanced age, or a clinical decision by the multidisciplinary tumor board based on an assessment of surgical risk versus benefit.

Pretreatment Assessment and Laboratory Parameters

Baseline evaluation included clinical examination, digital rectal examination, serum prostate-specific antigen (PSA) measurement, chest and abdominopelvic computed tomography (CT) and technetium-99 bone scintigraphy for staging. Laboratory analyses comprised complete blood count, liver and renal function tests and biochemical parameters. Pretreatment PSA values at diagnosis and subsequent PSA responses at 3 and 6 months after ADT initiation were systematically recorded.

Treatment Procedure and Pathological Evaluation

All patients received androgen deprivation therapy (ADT), either through luteinizing hormone-releasing hormone (LHRH) agonists or antagonists.The median duration of ADT was 24 months (range: 6–48 months), and there was no significant difference in ADT duration between HR and VHR groups (p=0.215). In addition, a subset of patients underwent definitive external beam radiotherapy with treatment fields including the prostate ± pelvic lymph nodes depending on disease extent and physician decision. Pelvic nodal radiotherapy (PNRT) was administered to 22 patients (27.2%; HR: 4/24, 16.7%; VHR: 18/57, 31.6%; p=0.173). Since no patients underwent radical prostatectomy,

pathological evaluation was limited to biopsy specimens. Gleason scores and Grade Groups were assigned according to the 2014 International Society of Urological Pathology (ISUP) consensus.[21]

Follow-Up Protocol

Patients were followed every 3 months during the first 2 years, every 6 months between years 3 and 5 and annually thereafter. Each visit included physical examination, serum PSA measurement and assessment of treatment-related side effects. Imaging studies (CT, MRI, or bone scan) were performed in cases of rising PSA or symptoms suggestive of recurrence/metastasis. Overall survival (OS) was defined as the time from treatment initiation to death from any cause. Disease-free survival (DFS) was defined as the time from treatment initiation to local recurrence, distant metastasis or death, whichever occurred first.

Ethical Considerations

The study was approved by the Ethics Committee of Van Training and Research Hospital (Approval ID: GOKAEK 2025–04-13, dated 09 May 2025). All procedures were performed in accordance with the Declaration of Helsinki. As this was a retrospective study based on anonymized data, the requirement for informed consent was waived by the Institutional Review Board, but patient confidentiality was strictly maintained.

Statistical Analysis

All statistical analyses were conducted using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). Categorical variables were summarized as frequencies and percentages, whereas continuous variables were expressed as mean ± standard deviation (SD) or median (minimum–maximum), depending on distribution. The normality of continuous variables was assessed using the Kolmogorov–Smirnov test. For group comparisons, the Chi-square test was applied to categorical variables, and the Mann–Whitney *U*-test was used for continuous variables not meeting normality assumptions.

Survival outcomes were evaluated using the Kaplan–Meier method, and survival curves were compared with the Log rank test. Overall survival (OS) was defined as the interval from initiation of androgen deprivation therapy (ADT) to death from any cause. Disease free survival (DFS) was defined as the time from ADT initiation to local recurrence, metastasis, or death, whichever occurred first. Median survival times and 95% confidence intervals (CIs) were reported.

To identify independent prognostic factors, univariate Cox proportional hazards regression analyses were first performed. Variables with a p-value < 0.05 in univariate testing were subsequently included in multivariate Cox models. Hazard ratios (HRs) with 95% CIs were calculated. The proportional hazards assumption was tested using Schoenfeld residuals and was not violated.

To exclude collinearity effects, variance inflation factors (VIFs) were examined, with values >5 considered problematic; all predictors in the final models demonstrated VIF values <2.0. The number of outcome events per variable in the multivariate models exceeded 10, meeting the EPV (events per variable) rule and ensuring model stability. Internal validation was performed by bootstrap resampling (1000 iterations), which demonstrated minimal optimism in hazard ratio estimates and confirmed model reproducibility within the study cohort. All statistical tests were two-tailed, and a p-value < 0.05 was considered statistically significant.

Results

The study population consisted of patients diagnosed with prostate cancer, with a mean age of 72.8 years and a mean Gleason score of 8.47, reflecting a population with high -grade and aggressive tumor biology. The mean PSA value at diagnosis was 58.1 ng/mL, consistent with high disease burden. Clinical staging (cT) revealed that 79% were in locally advanced stages (cT3 and cT4), and 70.4% were in the VHR group. During treatment, 53 patients (65.4%) received radiotherapy. After ADT, mean PSA was 9.91 ng/mL at 3 months and 2.45 ng/mL at 6 months, indicating treatment efficacy. Despite this, 43.2% developed local recurrence or metastasis during follow-up. Bone metastasis was the most common site (70.4%). Mortality was recorded in 40.7% of the cohort (Table 1).

Compared with HR patients, the VHR group had significantly higher PSA values at diagnosis (69.9 vs 30.1 ng/mL) and higher Gleason scores (8.95 vs 7.33) (p<0.001). VHR cases were almost entirely advanced stage (cT3–4), while most HR

Table 1 Cohort Characteristics: Baseline Demographic, Clinical, and Pathological Features

	Number	Percentage (%)
Mortality	33	40.7%
RT	53	65.4%
Risk group		
HR	24	29.6
VHR	57	65.4
cT Stage		
cT2	17	21%
cT3	43	53.1%
cT4	21	25.9%
Metastasis site		
Bone	19	70.4%
Bone, Lung	4	14.8%
Bone, Liver	3	11.1%
Bone, Distal Lymph Nodes	1	3.7%
	Mean±SD (Med)	**Med (Min-Maks)**
Age	72.8±7.4	72.5 (56.5–89.69)
PSA at diagnosis	58.1±40.3	47.0 (15–180)
PSA at 3rd month after ADT	9.91±22.4	1.80 (0–105
PSA at 6th month after ADT	2.45±5.7	0.50 (0–32)
Δ PSA after ADT	7.47±20.9	1 (−0.25–99)

Notes: Data are presented as number (n) and percentage (%), or mean ± SD (median). Percentages are calculated based on the total cohort (N=81). The "Risk group" row displays the distribution of patients across high-risk (HR) and very-high-risk (VHR) categories. Δ PSA represents the change in PSA level after initiation of ADT.
Abbreviations: PSA, prostate-specific antigen; ADT, androgen deprivation therapy; RT, radiotherapy; HR, high risk; VHR, very high risk; cT, clinical tumor stage; SD, standard deviation; Med, median.

patients (66.7%) were cT2 (p<0.001). Radiotherapy (RT) rates were similar between groups (HR: 15/24, 62.5%; VHR: 38/57, 66.7%; p=0.719). Correspondingly, the number of patients who did not receive RT was 9 in the HR group (37.5%) and 19 in the VHR group (33.3%) (p=0.719). PSA responses after ADT (PSA at 3 and 6 months, ΔPSA) were similar between groups (Figure 1). However, the VHR group had a significantly higher rate of local recurrence and metastasis (p=0.002) (Table 2). Mortality was also higher in the VHR group, though the difference did not reach statistical significance (p=0.061).

For the entire cohort, mean OS was 72.1 months in the VHR group and 97.1 months in the HR group (p=0.039). Among RT recipients, this difference persisted (HR: 104.5 months vs VHR: 75.1 months; p=0.032). In patients who did not receive RT, no significant OS difference was observed (p=0.470) (Figure 2). However, this analysis was likely underpowered due to the small sample size of the non-RT subgroup (n=28). DFS was 23.3 months in VHR versus 44.5 months in HR (p=0.026) (Table 3). Thus, VHR patients experienced disease progression much earlier despite treatment.

In multivariate Cox regression analysis adjusting for age, baseline PSA, Gleason score, and T stage, VHR classification remained an independent predictor of worse OS (HR 2.15, 95% CI 1.32–3.50, p=0.002) and DFS (HR 2.42, 95% CI 1.46–4.01, p=0.001).

Discussion

Prostate cancer encompasses a wide biological spectrum, from indolent low- risk cases to highly aggressive VHR tumors associated with early mortality.[1,22] NCCN guidelines highlight the importance of distinguishing HR and VHR categories, reflecting their different therapeutic needs.[5] This classification is not only theoretical but corresponds to clinically meaningful differences in disease behavior and survival.[23] Our study, analyzing a retrospective cohort of nonmetastatic HR and VHR patients managed with ADT ± RT, confirms that VHR classification carries significant prognostic weight.[10,23]

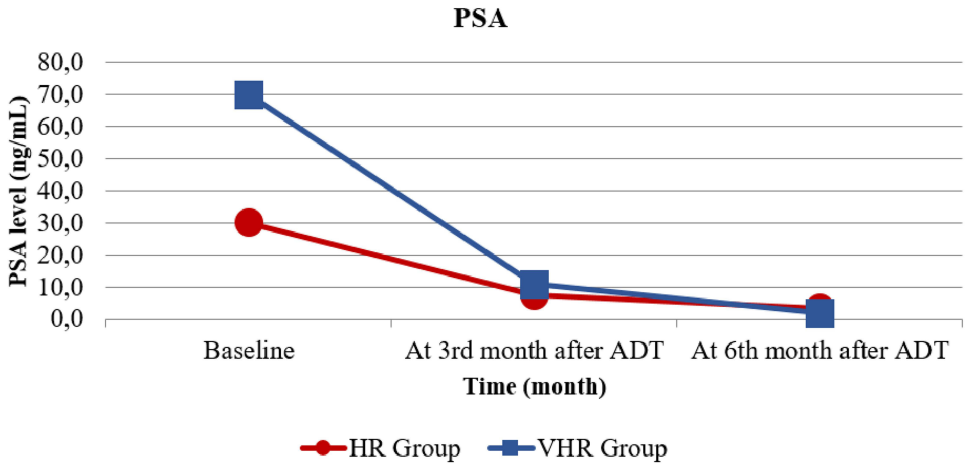

Figure 1 Change in prostate-specific antigen (PSA) levels over time in high-risk (HR) and very-high-risk (VHR) prostate cancer patients treated with androgen deprivation therapy (ADT). Line graph depicting mean PSA levels (ng/mL) at three time points: baseline (diagnosis), 3 months after initiation of ADT, and 6 months after initiation of ADT. The blue line represents the HR group (n=24), and the red line represents the VHR group (n=57). Error bars (if applicable) indicate standard deviation or standard error. The decline in PSA levels following ADT initiation is illustrated, with a more pronounced decrease observed in the VHR group at the 3-month time point.
Abbreviations: PSA, prostate-specific antigen; ADT, androgen deprivation therapy; HR, high risk; VHR, very high risk.

At baseline, VHR patients showed higher PSA levels, worse Gleason scores, and more advanced stages compared with HR patients.[24] This indicates that VHR disease represents more than a severe extension of HR; it is a distinct clinical and biological subgroup.[25] In line with Sundi et al (2014), who reported a threefold increase in metastasis risk and a sevenfold increase in cancer-specific mortality in VHR patients, our findings reinforce the aggressive nature of this classification.[10]

Table 2 Comparison of HR and VHR Groups Regarding Baseline Characteristics, Treatment Responses, and Recurrence/Metastasis Status

Risk Groups	**HR (n: 24)**	**VHR (n: 57)**	**P value**
Mortality	6 (25%)	27 (47.4%)	0.061
RT	15 (62.5%)	38 (66.7%)	0.719
PNRT	4 (27.2%)	18 (31.6%)	0.173
Recurrence/Metastatis status during follow-up	4 (16.7%)	31 (54.4%)	0.002
Local recurrence	1 (4.2%)	7 (12.3%)	0.264
Metastasis site			
Bone	2 (66.7%)	17 (70.8%)	0.732
Bone, Lung	1 (33.%)	3 (12.5%)	
Bone, Liver	-	3 (12.5%)	
Bone, Distal Lymph Nodes	-	1 (4.2%)	
	Mean±SD (Med)	**Mean±SD (Med)**	**P value**
Age	70.5±6.4 (71.1)	73.8±7.6 (72.9)	0.068
PSA at diagnosis	30.1±17.1 (19)	69.9±41.5 (55	**<0.001**
PSA at 3rd month after ADT	7.44±8.2 (4.4)	10.9±26.2 (1.2)	0.279
PSA at 6th month after ADT	3.54±5.6 (0.2)	1.98±5.7 (0.5)	0.4
Δ PSA after ADT	3.89±5.8 (1.5)	8.96±24.5 (0.8)	0.478

(*Continued*)

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Table 2 (Continued).

Risk Groups	HR (n: 24)	VHR (n: 57)	P value
cT Stage			**<0.001**
cT2	16 (66.6%)	1 (1.8%)	
cT3	8 (33.3%)	35 (61.4%)	
cT4	-	21 (36.8%)	

Notes: Categorical variables are presented as n (%). Continuous variables are presented as mean ± SD (median). P-values are derived from chi-square tests for categorical variables and independent t-tests or Mann–Whitney *U*-tests for continuous variables, as appropriate. Bold p-values denote statistical significance ($p < 0.05$). The percentage of HR patients receiving RT has been corrected to 62.5% (15/24). The "Metastasis site" subcategories are presented as proportions within the subset of patients who developed metastases.
Abbreviations: RT, radiotherapy; PNRT, pelvic nodal radiotherapy; PSA, prostate-specific antigen; ADT, androgen deprivation therapy; HR, high risk; VHR, very high risk; cT, clinical tumor stage; SD, standard deviation; Med, median.

One notable observation was that PSA declines during the first 3–6 months were similar in both groups, yet long-term survival diverged. This highlights that early biochemical response is not a reliable predictor of long-term outcomes.[26] Similar findings were reported by Zumsteg et al (2013) and Narang et al (2016), who showed that VHR patients, despite initial PSA responses, had much higher rates of biochemical failure and distant metastasis.[24,27] Our results are consistent with these reports.

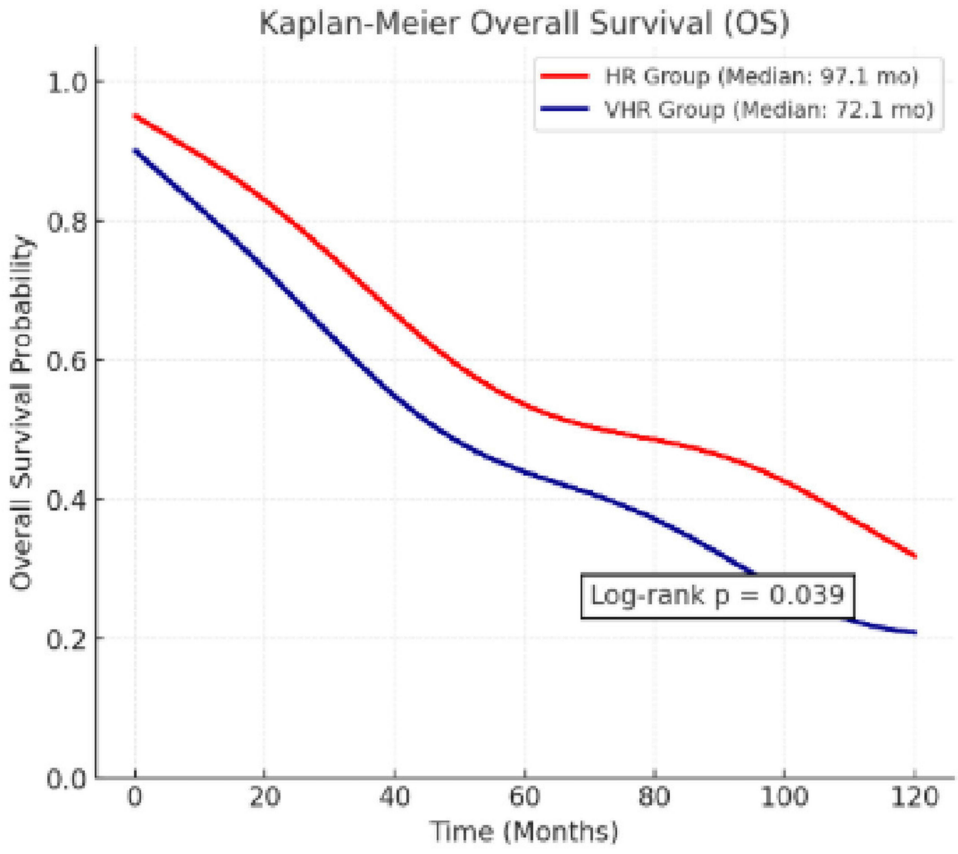

Figure 2 Kaplan–Meier curves for overall survival (OS) in high-risk (HR) versus very-high-risk (VHR) prostate cancer patients. Kaplan–Meier survival analysis comparing overall survival (OS) between the HR group (blue line, n=24) and the VHR group (red line, n=57). Median OS was 97.1 months for the HR group and 72.1 months for the VHR group. The Log rank test p-value is 0.039. The Y-axis represents the probability of overall survival, and the X-axis represents time in months. Shaded areas (if present) indicate 95% confidence intervals.
Abbreviations: OS, overall survival; HR, high risk; VHR, very high risk.

Table 3 Survival Outcomes: OS and DFS According to Risk Groups and Radiotherapy Status

	Mean	SE	%95CI		P value
			Lowest	Highest	
Risk Groups (OS)					
HR	97.1	8.3	80.8	113.5	**0.039**
VHR	72.1	4.4	63.5	80.8	
Overall Survival	77.9	4.2	69.6	86.2	
Risk group (OS) without RT					
HR	66.5	9.3	48.3	84.7	0.470
VHR	69.7	6.3	57.4	82.0	
Overall Survival	70.6	5.4	59.9	81.3	
Risk group (OS) with RT					
HR	104.5	9.5	85.9	123.1	**0.032**
VHR	75.1	6.9	61.4	88.8	
Overall Survival	77.9	4.2	69.6	86.2	
Risk Group DFS					
HR	44.5	**13.8**	17.5	71.5	**0.026**
VHR					
DFS Survival	25.7	2.6	20.6	30.9	
Risk group (DFS) without RT					
HR	66.8	0.0	66.8	66.8	0.080
VHR	24.7	3.9	17.2	32.3	
Overall Survival	27.7	4.7	18.6	36.9	
Risk group (DFS) with RT					
HR	37.1	16.4	4.9	69.3	0.195
VHR	22.3	2.5	17.4	27.2	
Overall Survival	24.4	3.1	18.4	30.5	

Notes: Survival times are presented in months. Mean survival, standard error (SE), and 95% confidence intervals (CI) are shown. P-values are derived from Log rank tests comparing survival curves between groups. Bold p-values denote statistical significance ($p < 0.05$). Analysis is stratified by receipt of radiotherapy (with RT/without RT).

Abbreviations: OS, overall survival; DFS, disease-free survival; HR, high risk; VHR, very high risk; RT, radiotherapy; SE, standard error; CI, confidence interval.

Median OS was significantly shorter for VHR patients (72.1 months) compared with HR (97.1 months, p=0.039). Among RT recipients, the gap persisted (75.1 vs 104.5 months, p=0.032). These findings clearly show inferior survival in VHR patients under non-surgical treatment.[23] Narang et al (2016) also reported worse outcomes for VHR across biochemical failure, distant metastasis, and cancer-specific mortality in patients treated with definitive RT plus ADT.[27] Likewise, Sundi et al (2014) reported 10-year metastasis-free survival of 78% in HR vs 37% in VHR, and prostate cancer-specific survival of 90% vs 62%.[10] These results align with the two-year OS gap seen in our study.

DFS also reflected this difference: 23.3 months for VHR versus 44.5 months for HR (p=0.026). In the RT subgroup, VHR disadvantage remained (22.3 vs 37.1 months), though sample size limited significance.[23] Narang et al (2016) found 10-year biochemical failure and distant metastasis rates of 54% and 35% in VHR, compared to 35% and 13% in HR patients.[27] These data mirror the shortened DFS in our cohort.

In our multivariate analysis, after adjusting for age, baseline PSA, Gleason score, and T stage, VHR classification remained significantly associated with worse OS (HR 2.15, p=0.002) and DFS (HR 2.42, p=0.001). The persistence of VHR as an independent poor prognostic factor even after multivariate adjustment underscores its clinical relevance beyond conventional staging parameters. This finding reinforces the concept that VHR represents not merely an aggregation of adverse features, but a distinct biological entity with inherent aggressive potential.

Recurrence/metastasis rates were much higher in VHR (54.4%) versus HR (16.7%) (p=0.002). This reinforces the observation that similar early PSA responses do not translate into equivalent long -term control.[28] Narang et al (2016) similarly noted that VHR patients often respond initially but progress quickly, likely due to micrometastatic disease at diagnosis.[27]

Importantly, the median duration of ADT in our cohort was 24 months, which aligns with the lower end of contemporary guideline recommendations (typically 2–3 years for high-risk disease).[29,30] While no significant difference in ADT duration was observed between HR and VHR groups, the overall adherence to guideline-recommended durations may have influenced outcomes and should be considered when interpreting the results.

Importantly, differences between HR and VHR persisted even among RT-treated patients. While RT+ADT improved survival in HR cases, it was insufficient for VHR, underscoring the need for treatment intensification.[11] Options may include prolonged ADT, brachytherapy boost, pelvic nodal RT, novel androgen receptor signaling inhibitors (ARSIs), or chemotherapy in selected cases.[12,13] This perspective is supported by multicenter series and increasingly by guideline recommendations.[22,25]

Some studies, however, questioned the discriminatory power of the VHR definition. For example, Saad et al (2017) reported limited separation between HR and VHR in a single-center RT cohort.[25] Yet, larger and methodologically stronger studies such as those by Sundi and Narang consistently support the value of the VHR classification.[10,27] Our findings are aligned with this body of evidence.[5]

In conclusion, our study, while limited by its retrospective design and potential selection bias, suggests that the HR–VHR distinction retains prognostic significance among non-surgically managed patients. VHR patients had inferior OS and DFS and higher recurrence rates, even within the RT subgroup. These findings underscore the aggressive biology of VHR disease and suggest that standard RT+ADT may be insufficient, highlighting the need to explore intensified treatment strategies in this population. Future prospective studies incorporating modern diagnostic tools and systemic therapies are warranted to validate these findings and refine treatment approaches.

Limitations

This study has limitations. Its retrospective, single-center design introduces selection bias and limits generalizability. The sample size (n=81), particularly in subgroup analyses, reduced power and may have obscured some differences, such as DFS in RT patients. Treatment heterogeneity was present: though all received ADT, duration and RT protocols (dose, field design) varied.

Furthermore, the reasons for omitting surgery (eg, comorbidities, patient preference) may have introduced a selection bias, as patients with significant non-oncological comorbidities have an inherently poorer overall survival prognosis, which could confound the comparison between HR and VHR groups.

Another limitation is the absence of modern systemic agents. During the study period, ARSIs (abiraterone, enzalutamide, apalutamide) and upfront docetaxel were not routinely available. Outcomes therefore reflect conventional ADT ±RT and may underestimate current results. Imaging tools such as PSMA-PET and advanced MRI, which now provide better staging, were also not consistently used, possibly underestimating occult disease.

Additionally, our definition of DFS included death from any cause. Given the advanced age of the cohort, this may have included non-cancer-related deaths, potentially influencing the DFS results.

Finally, biomarker analyses were not included, which could further refine HR vs VHR biology. Despite these limitations, our results align with larger multi-institutional studies, supporting the robustness and external validity of our findings.[27]

Institutional Review Board Statement

This study was approved by the Non-Interventional Clinical Research Ethics Committee of Van Training and Research Hospital (Approval ID: GOKAEK 2025-04-13, dated 09 May 2025). The requirement for informed consent was waived by the Institutional Review Board due to the retrospective nature of the study.

Data Sharing Statement

De-identified data underlying the findings can be made available from the corresponding author upon reasonable request and appropriate approvals.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest.

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