Original Article

DOI: 10.4274/uob.galenos.2022.2022.1.4

Bull Urooncol 2022;21(3):98-104

Investigation of Factors Influencing the Prognosis in Prostate Cancer Patients with Isolated Bone Metastasis

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Abstract

Objective: Bone metastases, which show a milder course compared with visceral disease, are among the most common metastatic sites in prostate cancer. In the present study, we aimed to investigate the prognostic factors that influence the survival time in the castration-sensitive phase in patients diagnosed with prostate adenocarcinoma with isolated bone metastasis.

Materials and Methods: The prognostic effects of the clinical (performance status, number of bone metastases) and laboratory parameters of a total of 217 patients, of whom the data could be accessed, on survival in the castration-sensitive phase were evaluated.

Results: Of the 217 patients included in our study, 144 (66.4%) were metastatic at presentation. The mean age of the patients was 68.4 (42-88) years. The mean follow-up duration was 44 months. Of our 217 patients, 125 (57.6%) were included in the castration-sensitive group and 92 (42.4%) in the castration-resistant group. In multivariate analyses; lactate dehydrogenase, alkaline phosphatase (ALP) levels and the number of bone metastases were independent prognostic factors with a strong correlation with time to castration-resistant prostate cancer. The evaluation of these three parameters within the framework of a prognostic index and subsequent risk stratification revealed median progression-free survival times of 91, 36, 20 and 12 months for the very low-risk, low-risk, intermediate-risk and high-risk groups, respectively.

Conclusion: Lactate dehydrogenase, ALP levels and the number of bone metastases were determined as strong and useful prognostic factors in predicting time to castration-resistant prostate cancer in metastatic prostate cancer.

Keywords: Bone metastasis, prostate cancer, prognostic factors

Introduction

Prostate cancer constitutes the second most frequent cause of cancer-related mortality in males (1). The bones are among the most common metastatic sites in prostate cancer. Most of the time, the patient loses the chance of curative treatment in the presence of bone metastasis (2). Although it is known that there is a strong interaction between cancer cells and the microenvironment in bone metastases, that osteocytes, which play a leading role in bone remodeling and formation, interact with cancer cells; the form and magnitude of this interaction is not yet elucidated (3,4). In the case of bone metastasis, bone mineralization due to elevated osteoblastic activity and, as an indicator of this, elevated alkaline phosphatase (ALP) levels are encountered (5). However, the induced osteoblastic activity leads to the formation of bones of low quality that are at risk of fracture (6).

Another common condition in cancer patients is anemia encountered at diagnosis or developing later (7). The prevalence of anemia was reported to vary between 19% and 75% across different cancer diagnoses (8). Among the proposed theses are that anemia diminishes treatment response by creating tumor hypoxia and that it causes an increase in angiogenesis (9). Anemia has been reported as a poor prognostic factor in prostate cancer (10). The risk of anemia increases approximately three-fold in patients receiving androgen deprivation therapy (ADT) in prostate cancer (11).

To date, many prognostic models have been produced that can predict the course of the disease in metastatic prostate cancer. The first model was developed by Glass et at. (12) in non-castrate metastatic prostate cancer patients based on performance status, prostate specific antigen (PSA) level, localization of bone metastases and Gleason score (GS). Later studies revealed ALP levels to be a significant indicator of overall survival (OS) (13). According to the current literature; a high GS, large tumor size, high ALP and PSA levels constitute an independent risk factor for bone metastasis (14). The scores that have been devised were mostly based on castration-resistant patients.

Cite this article as: Ebinç S, Oruç Z, Urakçı Z, Kaplan MA, Küçüköner M, Işıkdoğan A. Investigation of Factors Influencing the Prognosis in Prostate Cancer Patients with Isolated Bone Metastasis. Bull Urooncol 2022;21(3):98-104

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Received: 23.01.2022 **Accepted:** 02.03.2022

In this study, we aimed to investigate the prognostic factors that will predict the time to castration-resistant prostate cancer (CRPC) in patients diagnosed with prostate adenocarcinoma with bone-only metastasis in light of the literature and to assess the role of these factors in a prognostic index that will offer convenient clinical use.

Materials and Methods

In this study, data of patients diagnosed with prostate adenocarcinoma who presented to the Medical Oncology Clinic of Dicle University, Faculty of Medicine between 2010-2020 were retrospectively examined. In total, 349 (43.9%) of the 795 patients diagnosed with prostate cancer had metastatic disease. Of the patients who developed metastases, 132 (43.9%) had visceral organ metastasis and 217 (62.2%) had isolated bone metastasis. Our study included patients diagnosed with prostate adenocarcinoma with isolated bone metastasis. Patients with visceral organ metastases were not included in the study. The clinical characteristics of patients' [age, GS, number of bone metastases, Eastern Cooperative Oncology Group performance status (ECOG PS), lymph node metastasis], total PSA (tPSA), mean platelet volume (MPV), lactate dehydrogenase (LDH), ALP, hemoglobin (Hg) and albumin levels at diagnosis, treatments received during the hormone-sensitive phase were recorded. The relationships of these parameters in the castration-sensitive phase with time to CRPC were investigated.

Castration-resistant disease was accepted as; clinical, radiological and biochemical progression of the disease despite castration-level testosterone levels (<50 ng/dL). The diagnosis of metastatic disease was made using the following methods: Magnetic resonance imaging, computed tomography, bone scintigraphy or positron emission tomography/prostate-specific membrane antigen. Treatment response was evaluated every three months, based on clinical results, PSA levels and radiological imaging. Radiological response was evaluated according to the Response Evaluation Criteria in Solid Tumors criteria.

All analyses were performed in accordance with the principles of the Declaration of Helsinki. Approval was obtained from the Ethics Committee of Dicle University Medical Faculty for the study (decision number: 127, date: 25.02.2021).

Statistical Analysis

SPSS 18.0 package program was used for statistical analysis of the data. Descriptive statistics were used to evaluate patient characteristics and the frequencies of the parameters, student's t-test was used for normally distributed numeric variables, and the Mann-Whitney U test was used for the analyses of non-normally distributed variables. As ten clinical and laboratory parameters at the first metastatic diagnosis; age (15), tPSA (16), albumin (15), LDH (15), MPV (17), ALP levels (15), number of bone metastases (18), treatments received during the hormone-sensitive phase (19), GS (20) and ECOG PS (15) were defined as independent variables based on previous studies. The Kaplan-Meier method (Tarone-Ware tests, Breslow, Log-rank) was used for survival analysis. OS was calculated as the duration of time from the diagnosis to mortality, metastatic OS as the duration of time from metastatic progression to mortality, and time to CRPC as the duration of time from ADT initiation to the development of refractory disease. Receiver operating characteristic (ROC) analysis was used to determine cut-off values for the quantitative parameters with high sensitivity and specificity. In univariate analysis, chi-square test, the t-test, Mann-Whitney U tests and Fisher's Exact were used. The parameters that had prognostic significance in the univariate analysis were introduced to the Cox regression model to determine the parameters with prognostic value for time to CRPC in prostate cancer patients with isolated bone metastases. A 95% confidence interval and a p significance level <0.05 were adopted.

Results

This study included a total of 217 patients diagnosed with prostate adenocarcinoma who had isolated bone metastases. Of our patients, 125 (57.6%) were included in the castration-sensitive group and 92 (42.4%) in the castration-resistant group. One-hundred and forty-four patients (66.4%) were metastatic at initial diagnosis. Seventy-three patients (33.6%) who initially presented at a localized stage and later developed metastasis had received primary radiotherapy or radical prostatectomy at the localized stage. The mean age of the patients was 68.4±8.3 years. The median follow-up duration was 33 (2-217) months [32 (2-216) months for castration-sensitive patients and 34 (2-217) months for castration-resistant patients]. In the castration-sensitive phase, 198 (91.2%) patients were given ADT [bilateral orchiectomy or gonadotropin-releasing hormone agonist (leuprolide, goserelin) ± bicalutamide] and 19 (8.8%) patients were given ADT + docetaxel therapy. Hormone refractory disease occurred during the follow-up of our 125 (57.6%) patients. The baseline characteristics of the patients are presented in Table 1.

In patients who developed castration resistance, the median time to castration resistance was 25 months [95% confidence interval (CI): 20.6-29.3]. The median survival time from diagnosis was 42 months (95% CI: 32.1-51.8), the OS time from metastatic progression was 31 (95% CI: 26.0-33.9) months, the median survival time after the development of castration-resistance was 10 (95% CI: 8.6-11.4) months. For our patients in the castration-sensitive and castration-resistant groups, the median OS times from diagnosis were 51 months and 41 months (p=0.38), respectively. The median OS times from metastatic progression were 31 and 30 months (p=0.62). The progression-free survival times of our patients with the treatments given in the hormone-sensitive phase were 11 months (95% CI: 8.6-13.3) and 28 months (95% CI: 22.7-33.2) for patients who received ADT + Docetaxel and patients who received ADT alone (p<0.001), respectively. Of our 125 castration-resistant patients, 91 (41.9%) had received one-line, 27 (12.4%) had received two lines, 5 (2.3%) had received three lines of therapy.

ROC analysis results and cut-off values concerning the following identified clinical and laboratory variables are presented in Table 2: LDH, ALP, MPV, tPSA and number of bone metastases. Cut-off values were determined as follows: MPV ≥8 fl [Area under curve (AUC): 0.618 (0.239-0.698), p=0.005], LDH ≥300 U/L (AUC: 0.600 (0.519-0.681), p=0.018), ALP ≥140 U/L [AUC: 0.609 (0.529-0.690), p=0.010], tPSA ≥100 ng/dL (AUC: 0.634 (0.555-0.713), p=0.001), number of bone metastases ≥5 [AUC:

Table 1. Baseline characteristics of patients at initial of metastatic disease

Characteristic	All patients (n=217) n (%)	Castration resistant (n=125) n (%)	Castration sensitive (n=92) n (%)	P value
Age (years)				
Mean ± SD	68.4±8.3	68.1±8.7	68.7±7.9	0.91***
ECOG PS				**0.048***
0-1	178 (82)	97 (54.5)	81 (45.5)	
≥2	39 (18)	28 (71.8)	11 (28.2)	
Gleason score				0.728*
<8	112 (53.8)	65 (58)	47 (42)	
≥8	96 (46.2)	58 (60.4)	38 (39.6)	
Lymph node metastasis				**0.016***
Yes	79 (36.7)	54 (68.4)	25 (31.6)	
No	136 (63.3)	70 (51.5)	66 (48.5)	
Co-morbidities				0.818*
Yes	75 (34.6)	44 (58.7)	31 (41.3)	
No	142 (65.4)	81(57)	61 (43)	
First treatment options				0.318*
ADT	198 (91.2)	112 (56.6)	86 (43.4)	
ADT + docetaxel	19 (8.8)	13 (68.4)	6 (31.6)	
Lactate dehydrogenase (U/L)				**0.018****
Median (range)	252 (112-1845)	292 (135-1845)	237 (112-1837)	
Alkaline phosphatase (U/L)				**0.010****
Median (range)	126 (36-4541)	168 (49-2254)	102 (36-4541)	
Albumin (gr/dL)				0.95***
Mean ± SD	3.39±0.65	3.39±0.64	3.38±0.66	
Hemoglobin (gr/dL)				0.19***
Mean ± SD	12.3±2.1	12.1±2.1	12.5±2.1	
Baseline PSA level (ng/dL)				**0.001****
Median (range)	90 (0.1-5000)	100 (0.1-5000)	38 (1-4217)	
Mean platelet volume				**0.005*****
Mean ± SD	7.8±1.5	7.6±1.5	8.2±1.5	
Number of bone metastases				**<0.001****
Median (range)	5 (1-21)	6 (1-21)	3 (1-20)	

ADT: Androgen deprivation therapy, ECOG PS: Eastern Cooperative Oncology Group performance status *Chi-Square test, **Mann-Whitney U test ***Student t-test, SD: Standard deviation

0.648 (0.574-0.723), p<0.001]. Among these variables; number of bone metastases, ≥5, LDH ≥300 U/L, ALP ≥140 U/L, MPV ≤8fl and tPSA ≥100 ng/dL were determined as strong prognostic values.

Univariate analyses revealed a statistically significant difference between the castration-sensitive and -resistant groups in terms of the number of bone metastases, LDH, ALP, MPV and PSA levels and lymph node involvement; and multivariate analyses determined a statistically significant association between the number of bone metastases (p=0.002), LDH (p=0.003) and ALP (p=0.004) variables and time to CRPC (Table 1, Table 3).

These three parameters (number of bone metastases, ALP and LDH) were defined as independent factors predicting time to CRPC. The number of bone metastases, ALP and LDH parameters were evaluated within the framework of a prognostic index. Patients with five or more bone metastases were given a score of 1, those with fewer than five bone metastases were given a score of 0, those with an ALP level of 140 U/L or above were given a score of 1, those with an ALP level below 140 U/L were given a score of 0, those with an LDH level of 300 U/L or above were given a score of 1, those with an LDH level below 300 U/L were given a score of 0. When all scores were summed to obtain a total score; those with a score of 0 were categorized into the very low-risk group, those with a score of 1 into the low-risk group, those with a score of 2 into the intermediate-risk group, and those with a score

Table 2. ROC analysis results for cut-off value							
Variables	**Cut-off value**	**AUC**	**95% CI**	**P value**	**sensitivity**	**1-spesifity**	**State variable**
Mean platelet volume (fl)	≥8	0.618	0.239-0.698	**0.005***	0.494	0.327	Castration sensitive
Lactate dehydrogenase (U/L)	≥300	0.600	0.519-0.681	**0.018***	0.487	0.291	Castration resistant
Alkaline phosphatase (U/L)	≥140	0.609	0.529-0.690	**0.010***	0.539	0.291	Castration resistant
Baseline PSA level (ng/dL)	≥100	0.634	0.555-0.713	**0.001***	0.567	0.354	Castration resistant
Number of bone metastases	≥5	0.648	0.574-0.723	**<0.001***	0.675	0.413	Castration resistant
ROC: Receiver operating characteristic, AUC: Area under curve, CI: Confidence interval *statistically significant							

Table 3. Multivariate analysis of factors affecting time to castration resistant prostate cancer			
	Multivariate analysis		
Variables	**HR**	**95% CI**	**P value**
Performance status (0-1. ≥2)	1.043	0.650-1.674	0.862
Mean platelet volume (fl) (<8. ≥8)	0.855	0.561-1.302	0.465
Lactate dehydrogenase (U/L) (<300. ≥300)	1.939	1.244-3.023	**0.003***
Alkaline phosphatase (U/L) (<140. ≥140)	1.988	1.252-3.157	**0.004***
Baseline PSA level (ng/dL) (<100. ≥100)	1.092	0.695-1.715	0.703
Lymph node metastasis (No. yes)	1.155	0.776-1.719	0.479
Number of bone metastases (<5. ≥5)	2.066	1.313-3.250	**0.002***
First treatment options (ADT. ADT+ docetaxel)	1.489	0.739-3.001	0.265
*Statistically significant, ADT: Androgen deprivation therapy, HR: Hazard ratio, CI: Confidence interval, PSA: Prostate specific antigen			

of 3 into the high-risk group. The number of patients, whose complete data could be obtained, and who were included in the prognostic index, was 190. The distribution of the patients across risk groups was as follows: 56 (29.5%) patients in the very low-risk group, 44 (23.3%) in the low-risk group, 46 (24.2%) in the intermediate-risk group, and 22 (23.2%) in the high-risk group. Time to CRPC values of the groups when ordered from the very low-risk group to the high-risk group were 91, 36, 20 and 12 months, respectively (p<0.001). There was a statistically significant difference between the groups in terms of time to CRPC (Table 4, Figure 1). The percentage of patients who developed castration resistance over time in each risk group is shown as a scale (Figure 2).

Discussion

In light of the literature, we investigated in this study the clinical and laboratory parameters predicting time to CRPC in patients diagnosed with prostate cancer with bone metastasis that would offer ease of use in practice. As is known, ADT or, in patients with a high tumor burden, ADT + docetaxel/second generation antiandrogen therapies can be used as the initial treatment in metastatic castration-naive prostate adenocarcinoma (19). In all patients included in our study, castration was obtained with ADT in the metastatic period. Patients with a high tumor burden and without chemotherapy rejection or contraindications who had appropriate performance status [n=19, (8.8%)] were given ADT + docetaxel. Time to CRPC was 28 months in the group that received only ADT [n=198 (91.2%)], while it was

Table 4. Prognostic index for time to CRPC in castration sensitive prostate cancer with isolated bone metastases						
			Time to CRPC (months)			
Risk groups	**n=190**	**Total score**	**Median**	**95% CI**	**HR (95% CI)**	**P value**
Very low	56	0	91	34.1-147.8	Reference	**<0.001***
Low	44	1	36	15.4-56.5	1.883 (1.055-3.361)	**0.032***
Intermediate	46	2	20	15.0-24.9	4.693 (2.62-8.402)	**<0.001***
High	44	3	12	10.1-13.8	9.843 (5.363-18.065)	**<0.001***
LDH ≥300 U/L=1			**LDH <300 U/L=0**			
ALP ≥140 U/L=1			**ALP <140 U/L=0**			
NBM ≥5=1			**NBM <5=0**			
*Statistically significant, CRPC: Castration resistant prostate cancer, LDH: Lactate dehydrogenase, ALP: Alkaline phosphatase, NBM: Number of bone metastases, CI: Confidence interval, HR: Hazard ratio						

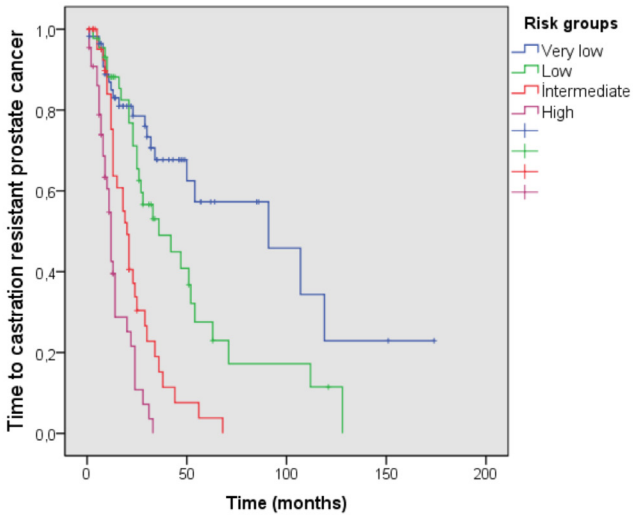

Figure 1. Time to castration resistant prostate cancer according to risk groups

Time to CRPC values of the groups when ordered from the very low-risk group to the high-risk group were 91, 36, 20 and 12 months, respectively (p<0.001)

CRPC: Castration-resistant prostate cancer

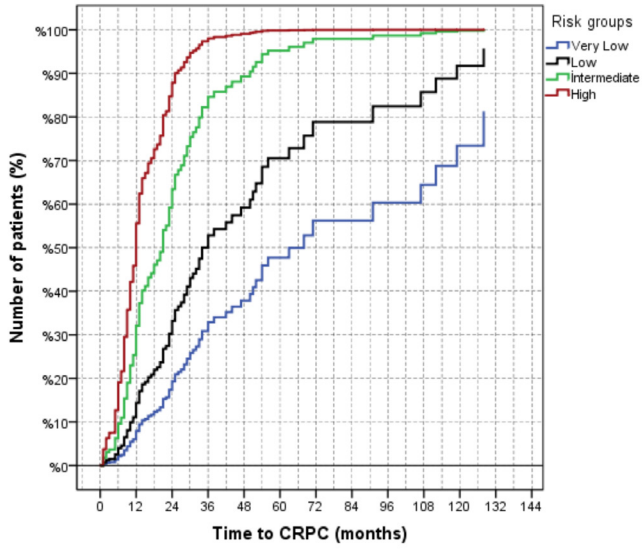

Figure 2. Castration resistant risk scale according to time

The percentage of patients who developed castration resistance over time in risk groups is shown on the scale

CRPC: Castration-resistant prostate cancer

11 months in the group that used ADT + docetaxel (p<0.001). There was a statistically significant difference between the two groups in terms of time to CRPC. We reasoned that this was because patients with a more aggressive clinical course and higher tumor burden were included in the chemotherapy arm.

Factors influencing survival, such as tumor metastasis sizes, radiological and laboratory parameters have been investigated in prostate cancer, particularly in the castration-resistant phase. In metastatic castration-resistant prostate cancer (mCRPC), the survival times for patients with only lymph node involvement, bone metastasis, lung and liver metastasis were reported as 31.6, 21.3, 19.4 and 13.5 months, respectively (21). Our study included prostate cancer patients with isolated bone metastases. For the patient group that remained castration-sensitive and the group that developed castration resistance, the median OS from diagnosis were 51 and 41 months, respectively (p=0.38). Meanwhile, the median OS from metastatic progression were 31 and 30 months for the two groups, respectively (p=0.62). There was no statistically significant difference between the two groups with regard to OS. However, the median survival times of our patients were longer compared with the values reported in the literature (21). Two-year and five-year biochemical progression-free survival rates of castration-sensitive patients were reported as 23- 64% and 6-31% (22). In our study, patients who developed castration resistance had a PFS of 25 months in the castration-sensitive phase. After the development of castration resistance, the median survival time of the patients in this group was 10 months.

The prediction of progression in castration-sensitive patients mostly involves genomic-based approaches such as Decipher (23) and Oncotype Dx (24). In the literature, prognostic factors such as a poor performance status, high LDH and ALP levels, low Hg and albumin levels, localization of bone metastases and presence of visceral organ metastasis were inspected predominantly in castration-resistant patients. OS values for risk groups were attempted to be estimated using nomograms in mCRPC patients (15).

When this matter is inspected along with the literature; it is found that 12- and 24-month survival rates and median OS times of patients with castration-resistant bone metastases were evaluated in a study by Fizazi et al. (16) using a nomogram including clinical and laboratory parameters such as skeletal-related events and the state of development of visceral metastasis, age, pain and performance status, time to first bone metastasis, Hg, ALP and PSA. In another study, it was reported that the volume of bone metastasis could be a prognostic marker of OS in mCRPC (25). Armstrong et al. (26) investigated the relationship between the automated bone scan index (BSI) and survival in CRPC patients with bone metastases in a prospective randomized study. In this study, ALP, PSA and LDH levels were determined to be correlated with the extent of bone involvement. There are also studies showing that the metastatic site, metastatic extent and pain are prognostic markers (27). In non-castrate metastatic prostate cancer; age, body mass index, pain status, Hg, LDH and ALP levels were reported to be prognostic markers indicating OS and, particularly, high ALP levels were found to be a strong predictor of OS (13).

With regard the castration-sensitive phase; Akamatsu et al. (28) evaluated the relationship of high LDH, GS, extent of disease with the OS in treatment-naive metastatic castration-sensitive prostate cancer and developed a risk stratification system. Besides GS, PSA and T-stage, other studies have also examined the BSI as an important prognostic marker during the ADT period (20) and as an independent predictor factor of time to

castration resistance (29). In a study conducted in Japan, Miyoshi et al. (30) constructed a nomogram involving age, T-stage, extent of the disease, GS and PSA levels in order to estimate 1-, 3- and 5-year survival in Japanese patients diagnosed with prostate cancer with bone metastasis. MPV, which is another parameter evaluated in the present study, has been studied in the literature as a prognostic marker in various diseases and was also evaluated in prostate diseases (31). However, it was not used as a prognostic marker in prostate cancer before. Studies have reported elevated MPV levels in males diagnosed with hypogonadotropic hypogonadism and reduced MPV levels in the presence of hyperandrogenemia in women diagnosed with polycystic ovary syndrome (17,32). This brings to mind the thesis that MPV is an indirect marker of androgen activity in the body.

In the present study, the parameters that have been used in the literature under various titles and, as described above, in different combinations, in order to predict the prognosis in prostate cancer were evaluated in prostate cancer patients with isolated bone metastases. As independent variables; we examined age, ECOG, PS, GS, tPSA, Hg, albumin, MPV, LDH, ALP, lymph node involvement and number of bone metastases.

In the evaluation of GSs and tPSA levels; no statistically significant difference was found between the castration resistant and castration-sensitive groups with regard to GSs (p=0.72), while PSA levels at metastatic onset were higher in the group that developed castration resistance, with statistical significance (p=0.001).

As specified in detail in Table 1; primarily, the number of bone metastases, MPV, ALP and LDH levels, as well as lymph node involvement and ECOG performance were significantly different between the groups in univariate analysis. Our results were consistent with the studies previously reported in the literature. MPV levels were lower in the castration-resistant group, with statistical significance. This appears to corroborate the studies reporting a relationship between androgens and MPV (17,32). In contrast with the nomograms reported in mCRPC patients in the literature; age, Hg and albumin levels were comparable between the castration-sensitive and -resistant groups in our study (15). When the prognostic parameters, for which cut-off values were determined using ROC analysis (Table 2), were evaluated using multivariate analyses, time to CRPC did not have a statistically significant correlation with ECOG PS, tPSA and MPV values. Number of bone metastases ≥5 (p=0.002), LDH ≥300 U/L (p=0.003), ALP ≥140 U/L (p=0.004) were statistically significant variables predicting time to CRPC in castration-sensitive metastatic prostate cancer. Excluding the parameters that did not have a statistically significant relationship with time to CRPC in multivariate analysis, the three parameters that were determined to have a strong statistical correlation with time to CRPC (number of bone metastases, LDH, ALP) were evaluated within the framework of an index. A score of 1 was recorded for each parameter meeting the following conditions: Number of bone metastases ≥5, LDH ≥300 U/L, ALP ≥140 U/L. When the total scores were computed from these three groups; the group with a score of 0 was defined as the very low-risk group, that with a score of 1 as the low-risk group, that with a score of 2 as the intermediate-risk group, and that with a score of 3 as the high-risk group. According to the comparison of these groups in terms of time to CRPC; the median time to CRPC values for the very low-, low-, intermediate- and high-risk groups were 91 months, 36 months, 20 months, 12 months, respectively (log rank p<0.001). There was a statistically significant difference between the groups in terms of ADT-T (Table 4, Figure 1). We observed that the number of bone metastases, ALP and LDH levels at diagnosis were important and strong prognostic factors predicting time to CRPC in non-visceral metastatic prostate cancer. The Chemohormonal Therapy Versus Androgen Ablation Randomized Trial for Extensive Disease in Prostate Cancer (CHAARTED) study reported that complementing ADT with chemotherapy was associated with a survival advantage in high-volume metastatic castration-sensitive prostate cancer (18). In the CHAARTED study, high-volume disease was defined as the presence of visceral metastasis or the presence of at least 4 bone metastases with one outside of the pelvis and/or vertebral column (18). For some patient groups with isolated bone metastasis and no visceral organ metastasis, the factors described in the CHAARTED study are not sufficient by themselves for the chemotherapy decision. Our view is that the parameters we determined in this study in castration-sensitive prostate cancer with isolated bone metastasis can serve as predictor factors in the planning of the treatment, particularly with respect to the risk groups. We think that these three useful parameters that are easily accessible in practice, which were evaluated within the framework of an index, can assist and guide clinicians in the management of the patients and the prediction of time to CRPC in castration-sensitive metastatic prostate cancer.

Study Limitations

The limitations of our study were that the study was single-centered and retrospective and the number of patients was small.

Conclusion

Prostate cancer is a prevalent disease at advanced ages and various factors such as performance status, co-morbidities, life expectancy and histological characteristics of the disease play a role in the planning of the treatment. There is a need for predictive and prognostic markers that will indicate survival in the castration-sensitive phase and determine the treatment approach in prostate cancer patients with isolated bone metastases. We believe that the prognostic index specified in this study, which is composed of the number of bone metastases, LDH and ALP levels will be a practical tool useful in the prediction of time to CRPC in prostate cancer patients with isolated bone metastases.

Acknowledgements

Publication: The results of the study were not published in full or in part in form of abstracts.

Contribution: There is not any contributors who may not be listed as authors.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

Ethics

Ethics Committee Approval: Approval was obtained from the Ethics Committee of Dicle University Medical Faculty for the study (decision number: 127, date: 25.02.2021).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: S.E., Z.O., Z.U., M.A.K., M.K., A.I., Design: Supervision: S.E., Z.O., Z.U., M.A.K., M.K., A.I., Data Collection-Processing: S.E., Z.O., Z.U., M.A.K., M.K., A.I., Analysis-Interpretation: S.E., Z.O., Z.U., M.A.K., M.K., A.I., Literature Review: S.E., Z.O., Z.U., M.A.K., M.K., A.I., Writing: S.E., Z.O., Z.U., M.A.K., M.K., A.I., Critical Review: S.E., Z.O., Z.U., M.A.K., M.K., A.I.

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