

Eastern Cooperative Oncology Group Performance Score Is Associated With Survival After Radiotherapy of Bone Metastases from Prostate Cancer

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Abstract. *Background/Aim:* Understanding prognostic factors of survival are important for treatment personalization in cancer patients. This study aimed to identify such factors for patients irradiated for bone metastases from prostate cancer. *Patients and Methods:* Data from 74 patients irradiated between 01/2009 and 04/2019 were retrospectively evaluated. Ten characteristics were investigated for survival. *Results:* Median survival in the entire cohort was 12 months. Survival rates at 3, 6, 9 and 12 months were 84%, 73%, 56% and 47%, respectively. On univariate analyses, the Eastern Cooperative Oncology Group (ECOG) performance score of 0-1 was associated with improved survival ($p < 0.001$), absence of visceral metastases ($p = 0.099$) and only one irradiated metastatic site ($p = 0.099$) showed a trend. On Cox regression analysis, only ECOG performance score (risk ratio = 3.58, $p < 0.001$) was significant. *Conclusion:* ECOG performance score is an independent prognostic factor of survival after irradiation of bone metastases from prostate cancer and may allow better personalization of care.

Up to 70% of prostate cancer patients experience bone metastases during the course of their disease (1). Many of these patients receive radiotherapy mainly to relieve pain and to stabilize bones affected by osteolytic lesions (2). For the irradiation of osseous metastases, several dose-fractionation regimens are administered worldwide, including single-

fraction radiotherapy, multifraction short-course programs (overall treatment time up to one week) and longer-course programs (usually lasting 2-4 weeks) (2). In cases of uncomplicated bone metastases, *i.e.* bone metastases without malignant spinal cord compression or an extensive soft-tissue component and/or an (impending) pathological fracture, single-fraction radiotherapy can be recommended for patients with a short survival time (2-4). Unfortunately, recurrent bone pain occurs significantly more often after single-fraction treatment compared to treatment with a multifraction regimen (2-4). Moreover, recalcification of osteolytic bone metastases is more prominent when multiple fractions are used (5). Since significant recalcification can only be expected after several months following radiotherapy, this endpoint is mainly important for patients with more favorable survival prognoses. Also, since the risk of a local recurrence of bone metastases associated with another episode of pain increases with time, this aspect should be considered when treating patients with longer-time expected survival (2-4). Thus, the optimal radiation program for a patient with bone metastases should take into account the predicted remaining lifespan. For predicting a patient's survival independent prognostic factors can be quite valuable. Since cancer types are different with respect to biology, prognosis and patterns of metastatic spread, it is generally agreed that independent prognostic factors should ideally be available for the different cancer types. This study was conducted to identify independent prognostic factors for survival after radiotherapy of bone metastases from prostate cancer.

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Key Words: Prostate cancer, bone metastases, multi-fraction irradiation, survival, prognostic factors.

Patients and Methods

The data of 74 patients irradiated for bone metastases from prostate cancer between 01/2009 and 04/2019 were retrospectively evaluated. This study was approved by the ethics committee of the University of Luebeck. All 74 patients received multi-fraction longer-course irradiation with i) 10x3 Gy in 2 weeks (n=31), ii) 12x3 Gy in 2.5 weeks (n=1), iii) 14-15x2.5 Gy in 3 weeks (n=32),

Table I. Distribution of the investigated factors.

	Number of patients (%)
Age at RT	
≤75 Years	34 (46)
≥76 Years	40 (54)
ECOG performance score	
0-1	40 (54)
≥2	26 (35)
Unknown	8 (11)
Interval from diagnosis of prostate cancer to RT of bone metastases	
≤24 Months	37 (50)
≥25 Months	37 (50)
Visceral metastases	
No	53 (72)
Yes	21 (28)
Further bone metastases	
No	6 (8)
Yes	68 (92)
Location of metastatic sites	
Spine	24 (32)
Extraspinal	28 (38)
Both	22 (30)
Number of irradiated sites	
1	30 (41)
≥2	44 (59)
Pathological fracture	
No	61 (82)
Yes	13 (92)
Upfront surgery of bone metastases	
No	66 (89)
Yes	8 (11)
Systemic treatment prior to RT	
No	9 (12)
Yes	64 (86)
Unknown	1 (1)

RT: Radiotherapy; ECOG: Eastern Cooperative Oncology Group.

iv) 15x2 Gy in 3 weeks (n=3) or v) 18-20x2.0 Gy in 3.5-4 weeks (n=7). The following ten characteristics (Table I) were investigated with respect to survival: i) age (≤75 vs. ≥76 years), ii) Eastern Cooperative Oncology Group (ECOG) performance score (6) (ECOG 0-1 vs. ≥2), iii) interval from diagnosis of prostate cancer to irradiation of bone metastases (≤24 vs. ≥25 months, median interval=24.5 months), iv) visceral metastases (no vs. yes) or v) further bone metastases (no vs. yes) prior to irradiation of bone metastases, vi) location of metastatic sites (spinal vs. extraspinal vs. both), vii) number of irradiated metastatic sites (1 vs. ≥2), viii) pathological fracture (no vs. yes), ix) upfront surgery of the bone metastases (no vs. yes) and x) previous systemic treatment prior to irradiation (no vs. yes).

Survival time was referenced from the start of irradiation of the bone metastases. For univariate analyses, the Kaplan-Meier method and the log-rank test were applied. Characteristics that were significant ($p < 0.05$) or showed at least a trend ($p < 0.10$) on univariate analyses were additionally investigated for independence in a multivariate Cox regression analysis.

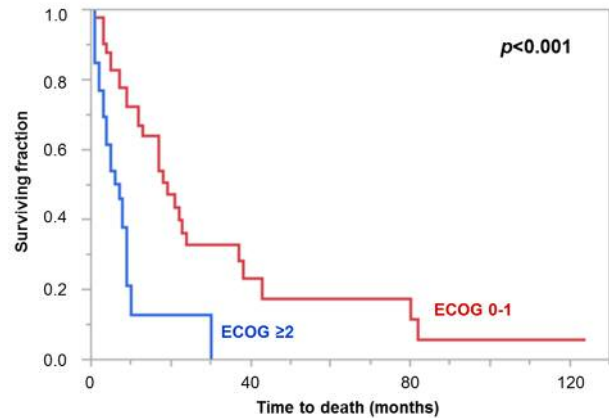


Figure 1. Kaplan-Meier curves for Eastern Cooperative Oncology Group (ECOG) performance scores of 0-1 vs. ≥2.

Results

Median survival in the entire cohort was 12 months. Survival rates at 3, 6, 9 and 12 months were 84%, 73%, 56% and 47%, respectively. On univariate analyses, an ECOG performance score of 0-1 was significantly associated with improved survival (Figure 1, $p < 0.001$). In the absence of visceral metastases ($p = 0.099$) and for only one irradiated metastatic site ($p = 0.099$), a trend towards better survival was found ($p = 0.099$). The data of the univariate analyses are summarized in Table II.

In the Cox regression analysis, the ECOG performance score (risk ratio=3.43, 95%-confidence interval=1.67-7.12, $p < 0.001$) achieved significance, whereas absence of visceral metastases (risk ratio=1.07, 95% confidence interval=0.54-2.05, $p = 0.83$) and one irradiated metastatic site (risk ratio=1.12, 95% confidence interval=0.59-2.11, $p = 0.73$) did not.

Discussion

Prostate cancer is the most common type of cancer in men in industrial nations (1). A considerable number of patients with prostate cancer develop metastases. To improve the prognoses of these patients, novel anticancer drugs have been introduced (7-10). Another approach aiming to improve their outcomes is through personalized care. Personalization of treatment should be based on the patient's individual situation, including his expected survival time. For the estimation of survival prognoses independent prognostic factors are very useful. For patients with prostate cancer, such factors have been identified for other metastatic situations, including brain metastases and malignant spinal cord compression (11-15). The current study was conducted to identify independent prognostic factors for prostate cancer patients with bone metastases.

Table II. Survival rates of the 11 potential prognostic factors (univariate analysis).

Factor	Survival rates (in %) at				p-Value
	3 months	6 months	9 months	12 months	
Age at RT					
≤75 Years	88	76	58	46	0.61
≥76 Years	80	70	54	49	
ECOG performance score					
0-1	90	83	72	67	<0.001
≥2	69	50	21	13	
Interval from diagnosis of prostate cancer to RT of bone metastases					
≤24 Months	89	73	59	48	0.66
≥25 Months	78	73	53	47	
Visceral metastases					
No	89	77	60	53	0.099
Yes	71	62	48	33	
Further bone metastases					
No	83	67	67	50	0.93
Yes	84	74	55	47	
Location of metastatic sites					
Spine	88	79	57	53	0.13
Extraspinal	79	68	54	46	
Both	86	73	58	42	
Number of irradiated sites					
1	83	77	70	63	0.099
≥2	84	70	46	36	
Pathological fracture					
No	82	72	55	48	0.37
Yes	92	77	60	43	
Upfront surgery of bone metastases					
No	83	73	57	49	0.23
Yes	88	75	45	30	
Systemic treatment prior to RT					
No	100	89	63	63	0.58
Yes	81	70	56	46	

RT: Radiotherapy; ECOG: Eastern Cooperative Oncology Group; bold p-values=significant.

The ECOG performance score was found to be independently associated with survival. This factor can aid physicians when personalizing treatment for patients with osseous metastases from prostate cancer.

Patients with a good performance status (ECOG score of 0-1) had a favourable prognosis with survival rates of 83% at 6 months and 67% at 12 months, respectively. Since many of these patients will live long enough to be at risk of experiencing another episode of bone pain in the irradiated regions, they may be considered for multi-fraction longer-course radiotherapy (2). According to previous meta-analyses, re-treating painful bone metastases was significantly less often required after longer-course than after single-fraction radiotherapy (3, 4). Moreover, in a prospective randomized trial, recalcification after longer-course treatment with 10x3 Gy given over 2 weeks was significantly stronger compared to single-fraction radiotherapy with 1x8 Gy (5). In this trial, the relative increases in bone density were 173% compared to 120% (p<0.001).

On the other hand, patients with a poor performance status (ECOG score of ≥2) had much less favorable survival rates of 50% at 6 months and only 13% at 12 months, respectively. In two large randomized trials of 1,171 and 765 patients, who were irradiated for painful bone metastases, recurrent bone pain occurred only after a median time of 11 months or >12 months, respectively (16,17). Most of the patients with an ECOG performance score of ≥2 will not live long enough to experience a second episode of bone pain and, therefore, appear suitable candidates for single-fraction radiotherapy. When following these considerations and suggestions, one should be aware of the retrospective nature of the data analyzed in this study that may have introduced a hidden selection bias. Although only patients receiving longer-course radiotherapy were included in this study to reduce the risk of a selection bias, the risk of hidden biases remained. Moreover, our suggestions may not be applicable to patients receiving single-fraction radiotherapy, since these patients were not included in the present study. Furthermore, one has to bear in mind that complicated bone metastases, *i.e.* bone metastases with an (impending) fracture, spinal cord compression or extensive soft-tissue component do generally require radiotherapy with multiple fractions (2).

In conclusion, the ECOG performance score was independently associated with survival. This prognostic factor can guide physicians when personalizing a dose-fractionation program for a patient with bone metastases from prostate cancer.

Conflicts of Interest

On behalf of all authors, the corresponding author states that there are no conflicts of interest related to this study.

Authors' Contributions

R.H., S.J., S.E.S and D.R. participated in the design of the study. R.H., S.J. and D.R. provided data. D.R. and S.E.S. performed the analyses of the data and drafted the manuscript, which has been reviewed and approved by all authors.

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