

Survival in Patients with Metastatic Spinal Cord Compression from Prostate Cancer Is Associated with the Number of Extra-spinal Organs Involved

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Abstract. *Background/Aim:* To investigate the predictive value of the number of extra-spinal organs involved by metastases for survival in metastatic spinal cord compression (MSCC) from prostate cancer. *Patients and Methods:* In 95 patients irradiated with 10×3 Gy for MSCC from prostate cancer, seven factors were investigated: Age, performance score, number of involved vertebrae, interval from prostate cancer diagnosis to MSCC, pre-radiotherapy ambulatory status, time to motor deficits development, number of involved extra-spinal organs. *Results:* Six-month survival rates for 0, 1 and ≥2 involved extra-spinal organs, were 81, 53 and 33%, respectively ($p<0.001$). On multivariate analysis, the number of involved extra-spinal organs maintained significance (risk ratio 1.88, $p=0.023$). Better performance score ($p<0.001$), longer interval from prostate cancer diagnosis to radiotherapy of MSCC ($p<0.001$), and being ambulatory prior to radiotherapy ($p=0.001$) were also positively associated with survival. *Conclusion:* The number of extra-spinal organs involved by metastases predicts survival in patients with MSCC from prostate cancer.

Prostate cancer is one of the most common primary tumors in patients presenting with metastatic spinal cord compression (MSCC) (1, 2). Radiotherapy (RT) alone is the most common treatment for this oncological emergency situation worldwide. The administered treatment regimen is influenced by the patient's survival prognosis. Because

single-fraction RT (e.g. 1×8 Gy) and short-course RT (e.g. 5×4 Gy in one week) regimens are similarly effective as longer-course programs (e.g. 10×3 Gy in two weeks or 20×2 Gy in four weeks) regarding pain relief and the improvement of motor deficits, patients with a short survival time appear optimally treated with single-fraction or short-course multi-fraction RT (3-6). It appears reasonable to keep the overall treatment time as short as possible for patients suffering from pain and neurological disorders. On the other hand, longer-course RT results in higher local control rates of MSCC than single-fraction or short-course regimens (6, 7). Local control of MSCC is particularly important for patients who survive long enough to develop a recurrence of MSCC in the previously irradiated parts of the spinal cord.

It is important to be able to estimate the patient's survival time in order to personalize care which is facilitated with a clear understanding of prognostic factors. A few independent predictors of survival have been identified for patients developing MSCC from prostate cancer including extra-spinal metastases (i.e. other bone and visceral metastases) (8). Until the present study only presence or absence of extra-spinal metastases was investigated as a prognostic factor but not the number of extraspinal organs involved by metastatic disease. However, the number of involved extra-spinal organs may be of prognostic value for survival. This study was therefore performed aiming to investigate the predictive value of the number of involved extra-spinal organs for the survival of prostate cancer patients receiving radiotherapy for MSCC from prostate cancer.

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Patients and Methods

Data of 95 patients treated with 10×3 Gy alone for MSCC from prostate cancer were retrospectively analyzed. 10×3 Gy has been the standard fractionation regimen at the contributing centers and is administered to the majority of patients with MSCC. Patients treated with fractionation regimens other than 10×3 Gy and patients

Table I. Patients' characteristics.

	Number of patients (%)
Age	
≤70 Years	44 (46)
>70 Years	51 (54)
ECOG Performance score	
1-2	32 (34)
3-4	63 (66)
Number of involved vertebrae	
1-2	27 (28)
≥3	68 (72)
Interval from cancer diagnosis to RT	
≤15 Months	37 (39)
>15 Months	58 (61)
Ambulatory status prior to RT	
Not Ambulatory	53 (56)
Ambulatory	42 (44)
Time to motor deficits development	
1-7 Days	33 (35)
8-14 Days	36 (38)
>14 Days	26 (27)
Number of involved extra-spinal organs	
0	26 (27)
1	57 (60)
≥2	12 (13)

ECOG: Eastern Cooperative Oncology Group; RT: radiotherapy.

receiving additional de-compressive surgery were not included in this study to minimize risk of a selection bias due to varying treatment approaches. Seven prognostic factors were analyzed for potential association with survival: Age (≤70 vs. ≥71 years, median age 71 years), Eastern Cooperative Oncology Group (ECOG) performance score (1-2 vs. 3-4), number of involved vertebrae (1-2 vs. ≥3), interval between the diagnosis of prostate cancer and RT of MSCC (≤15 vs. >15 months), pre-RT ambulatory status (not ambulatory vs. ambulatory), time to motor deficits development prior to RT (1-7 vs. 8-14 vs. >14 days), and number of extra-spinal organs involved by metastases (0 vs. 1 vs. ≥2 organs). Multiple metastases within the same organ system were counted as a single site. The patients' characteristics are presented in Table I. Univariate analyses of survival were performed with the Kaplan-Meier method and the log-rank test (9). Prognostic factors found to be significant in the univariate analysis ($p < 0.05$) were also evaluated in a multivariate analysis performed with the Cox hazards proportional model.

Results

In univariate analysis, improved survival was associated with an ECOG performance score of 1-2 ($p < 0.001$), involvement of only 1-2 vertebrae ($p = 0.003$), a time interval from first diagnosis of prostate cancer until RT of MSCC >15 months ($p = 0.001$), being ambulatory prior to RT ($p < 0.001$), a slower development (>14 days) of motor deficits ($p = 0.012$), and involvement of only 0-1 extra-spinal organs ($p < 0.001$).

Table II. Univariate analysis of survival.

	Survival at 6 months (%)	Survival at 12 months (%)	p-Value
Age			
≤70 Years	61	48	
>70 Years	55	45	0.79
ECOG Performance score			
1-2	94	87	
3-4	40	26	<0.001
Number of involved vertebrae			
1-2	78	68	
≥3	50	38	0.003
Interval from cancer diagnosis to RT			
≤15 Months	35	26	
>15 Months	72	60	0.001
Ambulatory status prior to RT			
Not Ambulatory	40	28	
Ambulatory	81	70	<0.001
Time to motor deficits development			
1-7 Days	42	34	
8-14 Days	50	41	
>14 Days	88	71	0.012
Number of involved extra-spinal organs			
0	81	81	
1	53	35	
≥2	33	22	<0.001

ECOG: Eastern Cooperative Oncology Group; RT: radiotherapy.

Results of the univariate analysis are summarized in Table II. In the multivariate analyses, the ECOG performance score ($p < 0.001$), the interval from first diagnosis of prostate cancer until RT of MSCC ($p < 0.001$), the pre-RT ambulatory status ($p = 0.001$), and the number of involved extra-spinal organs ($p = 0.023$) maintained significance. The time to motor deficits development prior to RT showed a trend ($p = 0.09$). While the number of involved vertebrae was not significantly associated with survival in the multivariate analysis ($p = 0.16$). The results of the multivariate analyses including the risk ratios and the 95%-confidence intervals are shown in Table III.

Discussion

In order to optimally treat patients in a palliative situation such as MSCC, a personalized treatment is the best approach possible. Such an approach objective must consider the patient's survival prognosis, which can be estimated with the help of independent prognostic factors and survival scores. For patients with MSCC from prostate cancer, several independent predictors of survival have been identified (8). In the specific

Table III. *Multivariate analysis of survival.*

	Risk ratio	95% CI	p-Value
ECOG Performance score	4.69	2.04-12.28	<0.001
Number of involved vertebrae	1.32	0.90-2.07	0.16
Interval from cancer diagnosis to RT	1.64	1.24-2.19	<0.001
Ambulatory status prior to RT	2.70	1.46-5.24	0.001
Time to motor deficits development	1.43	0.95-2.17	0.09
Number of involved extra-spinal organs	1.88	1.09-3.14	0.023

ECOG: Eastern Cooperative Oncology Group; RT: radiotherapy.

study, improved survival was significantly associated with a better performance status, being ambulatory status prior to RT, absence of other bone metastases, absence of visceral metastases, and with an interval between the first diagnosis of prostate cancer and RT of MSCC of >15 months. Based on these five independent prognostic factors, a survival score for patients with MSCC from prostate cancer was developed and validated (8). For each of the five prognostic factors, a separate score was created by dividing the 6-month survival rate (given in %) by 10. The prognostic scores were obtained from the sum of the scores for each factor and ranged from 30 to 39 points. According to the prognostic scores, three prognostic groups were designed. In the test group, the 6-month survival rates were 6.5% for 20 to 24 points, 44.6% for 26 to 33 points, and 95.8% for 35 to 39 ($p<0.001$). In the validation group, the corresponding 6-month survival rates were 7.4%, 45.4% and 94.7%, respectively ($p<0.001$). Therefore, this survival score was considered highly valid and reproducible. In this survival score, only the presence or absence was explored with respect to the prognostic factors visceral metastases and other bone metastases, whereas the number of extra-spinal organs involved by metastases was not evaluated. In addition to the study mentioned above, our present study investigated whether the number of involved extra-spinal organs, as well, is an independent prognostic factor for the survival of patients with MSCC from prostate cancer. Indeed, the present study found that patients with involvement of zero or only one extra-spinal organ, achieved significantly higher survival rates than patients with involvement of two or more extra-spinal organs, and these findings were consistent in the multivariate analysis. Despite the fact that the patients of the present study were treated homogeneously, a certain risk of a hidden selection bias still remains due to the retrospective nature of the data.

In addition to the number of extra-spinal organs involved by metastatic disease, improved survival was also significantly associated with a better performance status, longer interval from the first diagnosis of prostate cancer and RT of MSCC, and ambulatory status prior to RT. These

findings agree with the results of the previously mentioned study that identified independent predictors of survival in patients with MSCC from prostate cancer (8). Our results should ideally be confirmed in a prospective trial of MSCC from prostate cancer. However, trials that address this issue will not be available in the near future.

In conclusion, the number of extra-spinal organs involved by metastatic disease has shown to be an additional independent predictor of survival in patients with MSCC from prostate cancer. This prognostic factor may contribute to a better personalization of the treatment for these patients.

Conflicts of Interest

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

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