

Metastatic Spinal Cord Compression: A Survival Score Particularly Developed for Elderly Prostate Cancer Patients

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Abstract. *Aim: Metastatic spinal cord compression (MSCC) is an oncological emergency. Many elderly patients cannot tolerate intensive treatment and need individual approaches accounting for a patient's remaining lifetime. The goal of the present study was to develop a survival score for elderly prostate cancer patients with MSCC. Patients and Methods: Nine characteristics were analyzed in 243 patients: age, performance status, interval from prostate cancer diagnosis until MSCC, affected vertebrae, ambulatory status, further bone lesions, visceral metastases, time developing motor deficits, fractionation schedule. Results: Pre-radiotherapy ambulatory status ($p < 0.001$), visceral metastases ($p < 0.001$) and time developing motor deficits ($p < 0.001$) were significant for survival on Cox regression analysis and included in the survival score. Four groups were defined: 9-12, 13-16, 17-19 and 21-23 points. Six-month survival rates were 7%, 28%, 71% and 95%, respectively ($p < 0.001$). Conclusion: The present study identified four groups with different survival probabilities that require treatment strategies with different priorities ranging from symptom control to prolongation of life.*

Metastatic spinal cord compression (MSCC) is an oncological emergency that requires for immediate attention (1). Treatment of MSCC consists either of radiotherapy-alone or decompressive surgery followed by irradiation.

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Radiotherapy may be performed as conventional irradiation or stereotactic body radiation therapy (SBRT). Decompressive surgery is considered appropriate for about 15% of patients with MSCC but may be associated with complications such as bleeding and wound infection, thromboembolic events or pneumonia (1-3). The latter complications are more likely to occur in elderly patients. If SBRT is administered, the patients have to lie on the radiation couch for up to one hour and are generally not able to move during treatment. This may be burdensome particularly for elderly patients with severe pain.

Many elderly patients are not able to withstand intensive treatment of MSCC, such as decompressive surgery or SBRT (2-4). For selected elderly patients with a very favorable survival prognosis such intensive treatments may be a reasonable option to improve local control of MSCC when compared to conventional irradiation alone. However, the vast majority of elderly patients with MSCC are candidates for conventional irradiation rather than more intensive treatments.

If conventional radiotherapy is given, the most appropriate fractionation schedule, short-course or longer-course radiotherapy, has to be selected for each individual patient. Short-course was reported to be the optimal approach for patients with a poor survival prognosis (5). Patients with an intermediate prognosis are optimally treated with 3 Gy \times 10, over two weeks (5, 6). Patients with a more favorable prognosis should receive longer-course radiotherapy with total doses greater than 30 Gy, if decompressive surgery and SBRT are not possible or indicated (7).

These considerations demonstrate that it is crucial to understand the patient's survival prognosis as precisely as possible for choosing the best individual treatment strategy for MSCC. Survival scores do contribute significantly to the selection process. It has already been recognized that specific survival scores are required for single tumor entities such as

Table I. Survival of patients.

	At 6 months (%)	At 12 months (%)	p-Value
Age			
71-76 years (n=122)	64	52	
≥77 years (n=121)	53	40	0.38
ECOG performance score			
1-2 (n=107)	81	66	
3-4 (n=136)	41	31	0.27
Time from diagnosis of prostate cancer to irradiation of MSCC			
≤15 months (n=95)	71	58	
>15 months (n=148)	51	40	0.86
Number of affected vertebrae			
1-2 (n=94)	65	49	
3-4 (n=84)	58	49	
≥5 (n=65)	49	39	0.98
Pre-radiotherapy ambulatory status			
Not ambulatory (n=116)	34	25	
Ambulatory (n=127)	81	66	<0.001
Further bone metastases			
No (n=87)	71	58	
Yes (n=156)	51	40	0.40
Visceral metastases			
No (n=178)	70	56	
Yes (n=65)	26	15	<0.001
Time developing motor deficits			
1-7 days (n=72)	28	15	
8-14 days (n=74)	59	45	
>14 days (n=97)	80	69	<0.001
Fractionation schedule			
Short-course radiotherapy (n=144)	55	41	
Longer-course radiotherapy (n=99)	63	54	0.20

ECOG, Eastern Cooperative Oncology Group; MSCC, metastatic spinal cord compression. p-Values were obtained from Cox regression analysis.

breast cancer, lung cancer and prostate cancer (8-10). Furthermore, elderly patients have been identified as a particularly group of patients (11-15). Therefore, it is reasonable to create particular survival scores for elderly patients with MSCC from a single tumor entity. The current study aimed to develop such a score for elderly patients with MSCC from prostate cancer, one of the most common tumor types among patients presenting with MSCC.

Patients and Methods

Two hundred forty-three elderly patients aged ≥71 years treated with irradiation-alone for MSCC from prostate cancer were evaluated in this retrospective study. All patients had weakness of the lower extremities due to spinal cord compression and no prior local treatment of the involved segments of the spine. The fractionation schedule (short-course: 8 Gy × 1 or 4 Gy × 5 vs. longer-course: 3 Gy × 10, 2.5 Gy × 15 or 2 Gy × 20) and eight other characteristics

Table II. Significant characteristics and corresponding scoring points.

	Survival at 6 months (%)	Scoring points
Pre-radiotherapy ambulatory status		
Not ambulatory (n=116)	34	3
Ambulatory (n=127)	81	8
Visceral metastases		
No (n=178)	70	7
Yes (n=65)	26	3
Time developing motor deficits		
1-7 days (n=72)	28	3
8-14 days (n=74)	59	6
>14 days (n=97)	80	8

were investigated for associations with overall survival. These eight characteristics included age (71-76 vs. ≥77 years, median age=76 years), Eastern Cooperative Oncology Group (ECOG) performance score (1-2 vs. 3-4), time from initial diagnosis of prostate cancer until irradiation of MSCC (≤15 vs. >15 months), number of affected vertebrae (1-2 vs. 3-4 vs. ≥5), ambulatory status prior to irradiation (no vs. yes), further bone lesions before irradiation of MSCC (no vs. yes), visceral metastases before irradiation of MSCC (no vs. yes) and time developing motor deficits prior to start of irradiation (1-7 vs. 8-14 vs. >14 days).

All nine characteristics were evaluated regarding their impact on survival in a multivariate manner (Cox regression analysis). The characteristics that were deemed significant in the Cox regression analysis ($p < 0.0056$ after Bonferroni's adjustment for multiple tests representing an alpha level of 0.05) were included in the score designed for estimating the probability of surviving six months or longer following irradiation. The scoring points for each included characteristic were calculated by dividing the overall survival rate at six months by 10. The prognostic score for each individual patient was calculated by adding of the points of the significant characteristics.

Results

Three characteristics achieved significance for association with overall survival in the Cox regression analysis (Table I). These characteristics were the pre-radiotherapy ambulatory status (risk ratio (RR)=3.70; 95%-confidence interval (CI)=2.10-6.76; $p < 0.001$), presence of visceral metastases before irradiation of MSCC (RR=2.73; 95% CI=1.83-4.04; $p < 0.001$) and the time developing motor deficits prior to start of irradiation (RR=1.67; 95% CI=1.32-2.12; $p < 0.001$). Thus, these three characteristics were included in the survival tool. The scoring points of these characteristics are summarized in Table II. The total scores for individual patients and the corresponding 6-month survival rates are shown in Figure 1. Based on the total scores, four prognostic groups were defined: 9-12 points (group A, n=29), 13-16 points (group B, n=74), 17-19 points (group C, n=56) and

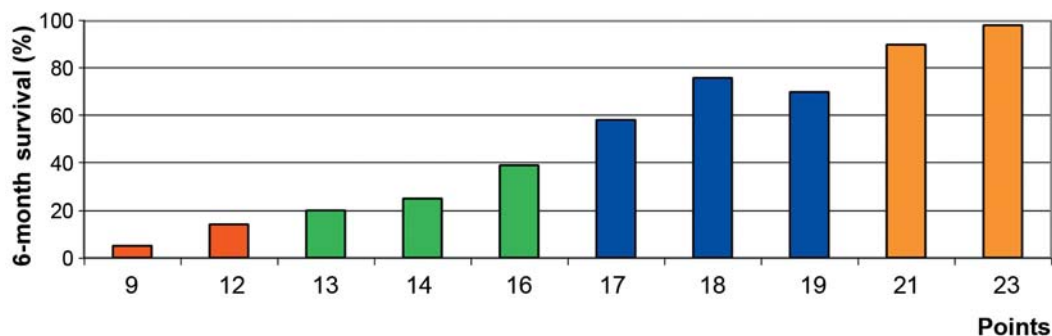


Figure 1. Six-month survival rates related to scoring points.

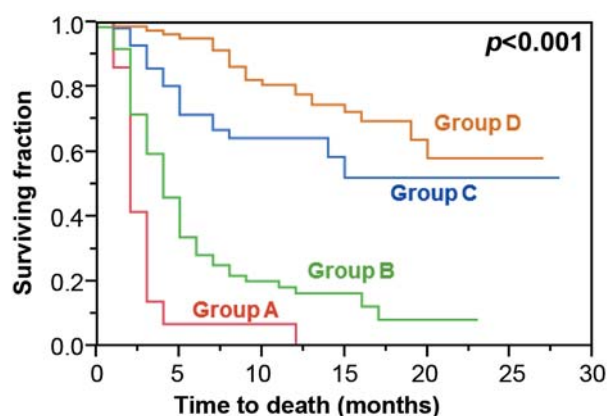


Figure 2. Kaplan-Meier curves of the four prognostic groups A (9-12 points), B (13-16 points), C (17-19 points) and D (21-33 points). The p -value was calculated with the log-rank test.

21-23 points (group D, $n=84$). The 6-month overall survival rates of the four groups were 7%, 28%, 71% and 95%, respectively ($p < 0.001$; Figure 2). The p -values were $p=0.037$ for the comparison of the 6-month survival probabilities of groups A vs. B, $p < 0.001$ for the comparison of groups B vs. C and $p < 0.001$ for the comparison of groups C vs. D, respectively (Chi-square test).

Discussion

Prostate cancer is one of the most common malignancies worldwide. Therefore, a great amount of research has been performed for both treatment of the primary tumor and treatment of disseminated disease including novel systemic agents and new radiotherapy technology (16-20). Prostate cancer patients account for approximately 20% of patients presenting with MSCC (1). Therefore, the group of patients with MSCC warrants particular attention. In recent years, elderly patients have been the focus of anticancer research

(11-15), since it has been recognized that these patients are a particular and growing group of cancer patients. Many elderly patients are less resilient to the effects of intensive anticancer treatments and, therefore, require for personalized treatment. In order to provide the optimal treatment for an individual elderly patient, such concepts should account for the patients' remaining lifetime. Estimation of the lifetime is possible by identifying significant prognostic factors and creating survival scores. To optimally meet the needs of elderly patients, this group requires specific scores, particularly in a palliative setting such as MSCC. Because tumor entities vary with respect to their biology and characteristics, ideally specific scores should also be available for different entities (8-10). Therefore, the present study was performed aiming to provide a survival score particularly designed for elderly patients with MSCC from prostate cancer.

According to the results of this study, three characteristics; pre-radiotherapy ambulatory status, presence of visceral metastases before irradiation of MSCC and the time developing motor deficits prior to start of irradiation, had a significant impact on survival. Based on these characteristics, four survival groups were identified with 6-month survival rates ranging from 7%-95%. Only 7% of the patients of group A (9-12 points) survived at least six months. Therefore, these patients are candidates for best supportive care or single-fraction (8 Gy \times 1) radiotherapy, which is the least burdensome and least time-consuming fractionation schedule showing similar effectivity as fractionated schedules (6, 7). Patients of group B (13-16 points) have a 6-month survival probability of only 28%. Therefore, these patients are good candidates for short-course multi-fraction treatment such as 4 Gy \times 5, since it is less time consuming but similarly effective with respect to improvement of motor function when compared to longer-course fractionation schedules (6, 7). Patients of group C (17-19 points) with a 6-month survival probability of 71%, respectively, should receive longer-course radiotherapy to provide better local

control of MSCC (5,6). The patients of group D (21-23 points) have the most favorable prognosis with a 6-month survival probability of 95% and a 12-month survival probability of 78%. These patients should receive longer-course radiotherapy with total doses beyond 30 Gy (2.5 Gy \times 15 or 2 Gy \times 20), since a previous study has shown that patients with a good survival prognosis benefit from doses greater than 30 Gy in terms of better treatment results (7). Selected patients of group D may also be considered for SBRT (4). Upfront decompressive surgery may be added to selected patients of the prognostic groups B, C and D with a good performance status and involvement by MSCC in only one spinal segment, particularly in case of sphincter dysfunction, vertebral fracture or spinal instability (1-3).

In conclusion, this new score enables one to estimate the survival probability of elderly patients with MSCC from prostate cancer. This score has a significant impact on the decision for personalized treatment approaches, in particular regarding the administration of decompressive surgery or SBRT as well as regarding the selection of the most appropriate schedule of conventional irradiation.

Conflicts of Interest

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

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