

# A Survival Score for Patients Assigned to Palliative Radiotherapy for Metastatic Bladder Cancer

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**Abstract.** *Aim: To create a survival score for patients with metastatic bladder cancer. Patients and Methods: In 46 irradiated patients, six characteristics were evaluated for their association with survival: Age, gender, Karnofsky performance scale, initial stage (American Joint Committee on Cancer), number of metastatic sites, and interval between bladder cancer diagnosis and palliative radiotherapy. Characteristics showing a trend ( $p < 0.15$ ) were incorporated into the score. Six-month survival rates were divided by 10. Patients' scores were derived by totaling the scores of these characteristics. Results: Performance scale ( $p = 0.14$ ), stage ( $p = 0.055$ ) and number of metastatic sites ( $p = 0.10$ ) showed a trend for association with survival. Patients' scores were 6, 7, 8, 10 or 12 points, with corresponding 6-month survival rates of 20%, 0%, 0%, 46% and 45% ( $p = 0.038$ ). Two groups were created, with 6-8 and with 10-12 points, with 6-month survival rates of 9% and 46% ( $p = 0.002$ ), respectively. Conclusion: A new survival score was developed. Patients with 6-8 points should receive less aggressive treatments for metastatic bladder cancer. Those with 10-12 points may receive more intensive approaches.*

Patients who present with metastatic bladder cancer generally have a poor prognosis, surviving only very few months (1). However, some patients may live considerably longer. If a patient is able to withstand palliative chemotherapy, their remaining lifetime may be extended with systemic treatments. Patients who are unable to tolerate chemotherapy are often referred to a radiation oncologist for palliative irradiation aiming to relieve or prevent debilitating

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symptoms (2, 3). In such palliative situations personalized treatment concepts account for the patient's preferences and needs, as well as their expected survival time.

Patients with a very short remaining lifespan should ideally not receive too intensive or time-consuming treatment programs. In contrast, patients with a much more favorable prognosis could benefit from more intensive approaches with higher total radiation doses. This concept was reported for radiotherapy of metastatic disease from other primary tumor types (4, 5). Tailoring a treatment program to an individual patient receiving palliative radiotherapy of metastatic bladder cancer during clinical routine would be easier if a simple tool was available allowing an estimation of such a patient's survival time. This study was conducted to develop such an instrument, specifically designed for patients irradiated for metastatic bladder cancer. Since a previous study suggested that the prognosis of these patients may be influenced by the radiation dose, only patients who received an equivalent dose in 2 Gy fractions (EQD2) of more than 30 Gy (6) were included.

## Patients and Methods

In 46 patients who received palliative radiotherapy with an EQD2 greater than 30 Gy for metastatic bladder cancer, six characteristics were retrospectively evaluated with respect to their impact on survival. The six characteristics (Table I) were age at palliative radiotherapy ( $\leq 70$  vs.  $> 70$  years, median = 70 years), gender, Karnofsky performance scale (KPS  $\leq 60\%$  vs.  $> 60\%$ , median KPS = 70%), initial tumor stage according to the American Joint Committee on Cancer (7) (AJCC stage  $\leq 3$  vs. 4, median = 3), number of organ sites involved by metastatic disease (1 vs.  $\geq 2$  sites, median = 1), and the interval between the first diagnosis of bladder cancer and palliative radiotherapy ( $\leq 12$  vs.  $> 12$  months, median = 13 months).

For the survival analyses, the Kaplan–Meier method was used supplemented by the log-rank test (8). Those characteristics having at least a trend towards an impact on survival ( $p < 0.15$ ) were incorporated into the survival score. For this score, the 6-month survival rates of the corresponding characteristics were taken and divided by 10. The prognostic score for a single patient was derived by adding the scores of all characteristics that showed a trend in the survival analysis.

Table I. Distribution of the six evaluated characteristics.

	Number of patients	Proportion (%)
Age at palliative radiotherapy		
≤70 Years	25	54
>70 Years	21	46
Gender		
Female	9	20
Male	37	80
KPS		
≤60	22	48
>60	24	52
Initial AJCC stage		
1-3	23	50
≥4	21	46
Unknown	2	4
Number of involved metastatic sites		
1	27	59
≥2	19	41
Interval between diagnosis of bladder cancer and palliative radiotherapy		
≤12 Months	22	48
>12 Months	24	52

AJCC: American Joint Committee on Cancer (7); KPS: Karnofsky performance scale.

Table II. Three- and 6-month survival rates of the evaluated characteristics.

	At 3 months (%)	At 6 months (%)	P
Age at palliative radiotherapy			
≤70 Years	56	36	0.22
>70 Years	43	19	
Gender			
Female	44	22	0.73
Male	51	30	
KPS			
≤60	45	18	0.14
>60	54	38	
Initial AJCC stage			
1-3	52	39	0.055
≥4	52	19	
Unknown			
Number of involved metastatic sites			
1	56	37	0.10
≥2	42	16	
Interval between diagnosis of bladder cancer and palliative radiotherapy			
≤12 Months	59	23	0.90
>12 Months	42	33	

AJCC: American Joint Committee on Cancer (7); KPS: Karnofsky performance scale.

**Results**

On survival analysis, KPS ( $p=0.14$ ), initial AJCC stage ( $p=0.055$ ) and number of sites involved by metastatic disease ( $p=0.10$ ) showed a trend towards an association with survival (Table II) and were, therefore, incorporated into the scoring tool.

The scores in relation to these characteristics are presented in Table III. Scores for single patients were 6, 7, 8, 10 or 12 points. The corresponding 6-month survival rates were 20%, 0%, 0%, 46% and 45%, respectively ( $p=0.038$ ; Figure 1). Based on these survival rates, two prognostic groups were created, with 6-8 points and with 10-12 points. The corresponding 6-month survival rates of these two groups were 9% and 46%, respectively ( $p=0.002$ , Figure 2).

**Discussion**

About every fourth patient with bladder cancer develops distant metastases during the course of their disease (9). Most of these patients have a poor prognosis that urgently requires improvement. On one hand, this may be achieved with chemotherapy programs or novel targeted therapies, such as agents that have an effect on the phosphatidylinositol-3-kinase–protein kinase B pathway, and other modern

Table III. Characteristics incorporated in the score and corresponding scoring points.

	Survival rate at 6 months (%)	Scoring points
KPS		
≤60	18	2
>60	38	4
Initial AJCC stage		
1-3	39	4
≥4	19	2
Unknown		
Number of involved metastatic sites		
1	37	4
≥2	16	2

AJCC: American Joint Committee on Cancer (7); KPS: Karnofsky performance scale.

approaches of systemic treatments (10-13). Personalized medicine is another promising approach to improving the prognosis of patients with metastatic cancer, including those with metastases from bladder cancer. To optimally utilize personalized anticancer treatment, the treating physicians have to be able to estimate an individual patient’s remaining

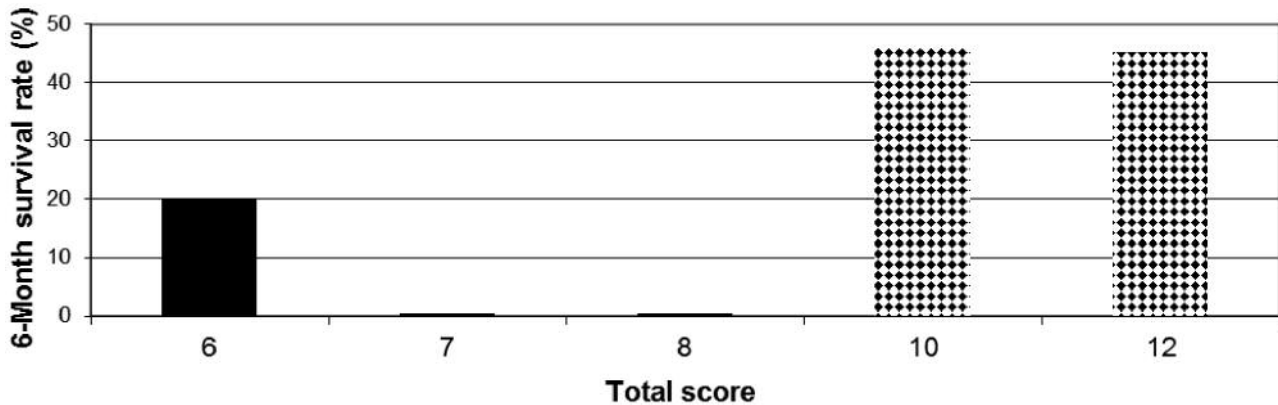


Figure 1. The 6-month survival rates obtained from the Kaplan–Meier analysis in relation to the scores calculated for each single patient.

lifespan as precisely as possible. To achieve this goal, precise knowledge of predictors of survival is very helpful. Moreover, a simple scoring tool that can easily be used in clinical routine is desirable to allow a quick and appropriate selection of an optimal treatment approach for an individual patient.

In the current study, such a tool was created for patients who received palliative radiotherapy for metastatic bladder cancer. Based on three potential prognostic factors, namely KPS, initial AJCC stage and the number of sites involved by metastatic disease, we derived two prognostic groups with significantly different 6-month survival rates. Patients with a total score of 6-8 had a 6-month survival rate of only 9%. Therefore, these patients can be considered candidates for a short and less intensive radiotherapy program. Several studies of palliative radiotherapy for metastases from solid tumors including bladder cancer have shown that a significant relief of symptoms can be achieved also with short radiotherapy programs that last only one day or one week. This has for example been demonstrated already for irradiation of painful bone metastases, metastatic spinal cord compression and brain metastases (2, 3, 14-17).

In the group of patients who achieved a score of 10-12 in the present study the 6-month survival rate was 46%, *i.e.* much better than in the groups with 6-8 points. Therefore, these patients may be considered for longer-lasting radiotherapy programs including higher total doses greater than 30 Gy. Previous studies of palliative radiotherapy for metastatic spinal cord compression and brain metastases have shown that patients with a better survival prognosis benefit from higher doses in terms of improved local control and survival (4, 5). When following these recommendations, one should be aware of the limitations of the present study, namely its retrospective nature and the

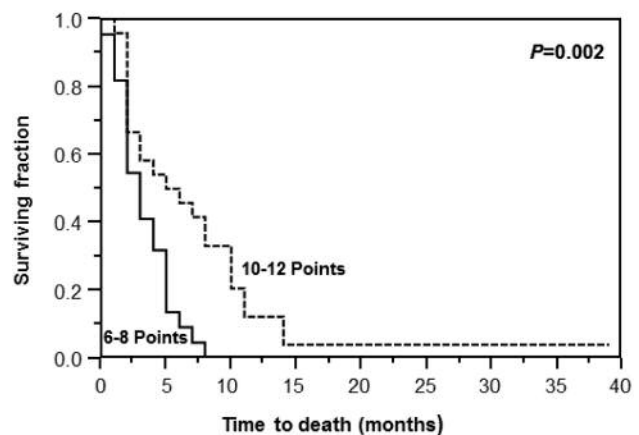


Figure 2. Kaplan–Meier curves of the overall survival of the two prognostic groups: with 6-8 points and 10-12 points (*p*-value obtained from log-rank test).

relatively small number of patients. Retrospective studies bear a certain risk of including hidden biases. In order to reduce the risk of bias, only patients receiving an EQD2 of more than 30 Gy were included in this study (6). Ideally, the results would be confirmed in a prospective trial. However, since patients with bladder cancer account for only about 2% of all patients with cancer, such a prospective trial with an adequate statistical power cannot be expected soon (18).

In summary, a new survival score was developed for patients receiving palliative radiotherapy for metastatic bladder cancer. Patients who achieve 6-8 points should receive less burdensome and less time-consuming treatments. In patients achieving 10-12 points, more intensive approaches may result in better local control and survival.

## Conflicts of Interest

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

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