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The Results of Whole-brain Radiotherapy for Elderly Patients With Brain Metastases from Urinary Bladder Cancer

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Abstract. *Background/Aim: The number of elderly patients with cancer is growing and requires particular attention. These patients may benefit from personalized treatments. This study aimed to identify prognostic factors of survival for elderly patients (≥65 years) irradiated for brain metastases from urinary bladder cancer. Patients and Methods: In 29 elderly patients treated with whole-brain radiotherapy (WBRT), seven factors were retrospectively analyzed regarding survival, namely dose-fractionation regimen, age, gender, Karnofsky performance score, number of brain metastases, extra-cranial metastases, and interval between cancer diagnosis and WBRT. Results: For the whole series, survival was 38% at 3 months and 21% at 6 months. Karnofsky performance score ≥70% showed a trend for being associated with improved survival when compared to ≤60%; survival rates were 50% vs. 29% at 3 months and 33% vs. 12% at 6 months (p=0.18). Conclusion: Karnofsky performance score may help estimate the survival of elderly patients irradiated for brain metastases from urinary bladder cancer.*

Of patients with solid tumors developing brain metastases during the course of their disease only ≤2% have a malignant tumor of the urinary bladder (1, 2). A considerable number of patients with urinary bladder cancer belong to the age group ≥65 years (elderly patients). Because of demographic changes, this group is constantly growing and, therefore, requires particular attention (1). Since many of these patients present with a reduced performance score and several co-morbidities, they may not be able to tolerate aggressive treatments. Personalization of the treatment can help tailor the treatment to a patient's situation, optimally matching therapy to the patient's needs. It is important that a personalized treatment approach for patients with brain metastases should consider a patient's survival prognosis (3). Estimation of survival is facilitated with the knowledge of corresponding prognostic factors. This study aimed to identify prognostic factors for survival for elderly patients (age ≥65 years) irradiated for brain metastases from cancer of the urinary bladder.

Patients and Methods

Twenty-nine elderly patients (age ≥65 years) treated with whole-brain radiotherapy (WBRT) alone for brain metastases from cancer of the urinary bladder were included in this retrospective study, which was approved by the Ethics Committee of the University of Lübeck (reference number: 19-011A). In this cohort, seven potential prognostic factors were analyzed for associations with survival. Some patients had already been included in previous studies (4, 5). The seven investigated factors were the dose-fractionation regimen (20 Gy in 5 fractions *vs.* 30 Gy in 10 fractions *vs.* 35-40 Gy in 14-20 fractions), age at WBRT (≤75 *vs.* ≥76 years; median=76 years), gender, Karnofsky performance score of ≤60 *vs.* ≥70%; median=60%), number of brain metastases (single *vs.* multiple), extra-cranial metastases (no *vs.* yes), and the time interval between diagnosis of urinary bladder cancer and WBRT (≤18 *vs.* ≥19 months; median=18 months). The distribution of these potential prognostic factors is shown in Table I. Survival analyses were performed using the Kaplan–Meier method and the log-rank test.

Results

For the whole series, survival was comparably poor following WBRT, with survival rates of 38% at 3 months and 21% at 6 months, and a median survival time of 2 months. On survival anaysis, a Karnofsky performance score of ≥70% showed a trend for being associated with improved survival when compared to a score of ≤60%. The survival rates were 50% *vs.* 29% at 3 months and 33% *vs.* 12% at 6 months, respectively (p=0.18, Figure 1). The results of the complete survival analyses are summarized in Table II.

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Key Words: Urinary bladder cancer, elderly patients, brain metastases, whole-brain radiotherapy, survival prognosis.

Table I. *Distribution of potential prognostic factors.*

Factor	Number of patients (%)
Dose-fractionation regimen	
20 Gy in 5 fractions	8 (27.6)
30 Gy in 10 fractions	13 (44.8)
35-40 Gy in 14-20 fractions	8 (27.6)
Age at WBRT	
≤75 Years	14 (48.3)
≥76 Years	15 (51.7)
Gender	
Female	6 (20.7)
Male	23 (79.3)
Karnofsky performance score	
≤60%	17 (58.6)
≥70%	12 (41.4)
Number of brain metastases	
Single	3 (10.3)
Multiple	26 (89.7)
Extra-cranial metastases	
No	4 (13.8)
Yes	25 (86.2)
Interval between diagnosis of bladder cancer and WBRT	
≤18 Months	15 (51.7)
≥19 Months	14 (48.3)

WBRT: Whole-brain radiotherapy.

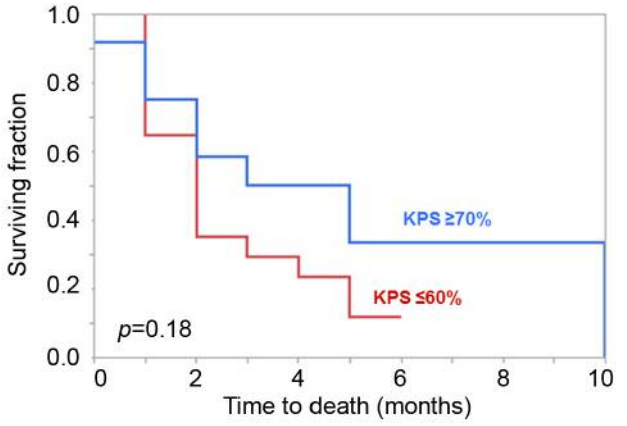

Figure 1. *Kaplan-Meier curves for survival of patients with a Karnofsky performance score (KPS) of ≥70% and those with a KPS of ≤60%. The p-value was calculated with the log-rank test.*

Discussion

Despite increasing research, the prognoses of patients with advanced cancer of the urinary bladder are generally poor and require improvement (1, 6-9). This applies particularly to elderly patients, whose health is often impaired by significant co-morbidities. A considerable number of these patients develop brain metastases. Despite increasing use of radiosurgery alone for patients with a limited number of cerebral lesions, many elderly patients with brain metastases from urinary bladder cancer still receive WBRT. This is because either they have multiple cerebral lesions at the time of diagnosis or may not tolerate radiosurgery due to their reduced performance score. When treating elderly patients, particular attention should be paid, since there often is only a narrow window between over-treatment associated with unnecessary toxicity and under-treatment possibly leading to poorer survival (2). Therefore, these patients require personalized treatment. Such treatment should take into account several aspects, including the patient's survival prognosis. In order to design an optimal treatment plan for a patient, it is important to know their remaining lifespan as precisely as possible. For estimation of the lifespan, prognostic factors are very helpful. Since different cancer types exhibit different biological behavior and are associated with different prognoses, it is important to know the specific prognostic factors for each type of cancer (10-14). The present study was performed to identify specific prognostic factors for elderly patients with brain metastases from urinary bladder cancer. Of the seven investigated factors, the Karnofsky performance score tended to be associated with survival. Although significance was not reached, the differences in 3- and 6-month survival were substantial, *i.e.* 21% at both points in time. These differences were even more prominent than in a previous study including patients of all age groups with brain metastases from urinary bladder cancer (5). In that previous study, the 3- and 6-month survival rates were 44% and 31%, respectively, in patients with a Karnofsky performance score of ≥70% *vs.* 44% and 22%, respectively, in those with a Karnofsky performance score of ≤60%. Taking into account the results of the current study, the Karnofsky performance score may support physicians who wish to estimate the survival of elderly patients with brain metastases from urinary bladder cancer. Since only 12% of the patients with a performance score of ≤60% survived for 6 months or longer, such patients with poor performance status should probably receive short-course WBRT with 20 Gy in 5 fractions over 1 week to avoid spending more time than necessary receiving treatment (2). In a prior analysis, for patients with less favorable survival prognoses, 20 Gy in 5 fractions was not inferior to longer-course WBRT with higher doses regarding intracerebral control and survival (15). In the present study, 20 Gy in 5 fractions was the shortest regimen used, and the dose-fractionation regimen had no significant impact on survival. In contrast, patients with better performance status ≥70% should be considered for longer regimens,

Table II. *Survival rates at 3 and 6 months following whole-brain radiotherapy.*

	At 3 months (%)	At 6 months (%)	*p*-Value
Dose-fractionation regimen			
20 Gy in 5 fractions	38	25	0.92
30 Gy in 10 fractions	38	15	
35-40 Gy in 14-20 fractions	38	25	
Age at WBRT			
≤75 Years	29	14	0.39
≥76 Years	47	27	
Gender			
Female	33	17	0.81
Male	39	22	
Karnofsky performance score			
≤60%	29	12	0.18
≥70%	50	33	
Number of brain metastases			
Single	33	33	0.55
Multiple	38	19	
Extra-cranial metastases			
No	25	25	0.75
Yes	40	20	
Interval between diagnosis of bladder cancer and WBRT			
≤18 Months	40	20	0.97
≥19 Months	36	21	

WBRT: Whole-brain radiotherapy.

since the 6-month survival rate was 33%. Lower doses per fraction have been found to lead to fewer neurocognitive deficits, which usually become evident only a few months after WBRT (16). When interpreting the present study's results, the comparatively small sample size and the retrospective design need to be considered.

In conclusion, the Karnofsky performance score may help estimate the survival time of elderly patients irradiated for brain metastases from cancer of the urinary bladder and contribute to personalization of their treatment.

Conflicts of Interest

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

Authors' Contributions

D.R., T.N. and S.E.S participated in the design of the study. D.R. and T.N. provided the data. D.R. and S.E.S. performed the analyses of the data and drafted the article, which has been reviewed and approved by all Authors.

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