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Estimating the Lifespan of Elderly Patients With Cerebral Metastases from Kidney Cancer

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Abstract. *Background/Aim: Outcomes of elderly patients with cerebral metastases from kidney cancer may be improved by personalized treatment. A scoring instrument for estimating survival in these patients is presented. Patients and Methods: Twenty-four elderly kidney cancer patients receiving whole-brain irradiation (WBI) were retrospectively investigated. WBI-regimen and six pre-treatment factors were evaluated including age, gender, performance score, number of cerebral metastases, extracranial metastases and time from kidney cancer diagnosis to WBI. Results: Number of cerebral metastases (p=0.194) and time from kidney cancer diagnosis to WBI (p=0.107) correlated with survival and were included in the instrument. Based on these factors, patient scores of 0, 1 and 2 points resulted in 6-month survival rates of 0%, 15% and 60% (p=0.131), respectively. Two groups were designed, 0-1 and 2 points, with 6-month survival rates of 11% and 60% (p=0.108), respectively. Conclusion: This new instrument can assist physicians aiming to estimate a patient's survival prognosis to provide personalized treatment.*

Approximately 10% of patients with kidney cancer develop cerebral metastases, and kidney cancer accounts for about 4% of solid tumors associated with cerebral metastases in adult cancer patients (1, 2). Many patients with a limited number of cerebral metastases (mainly defined as 1-3 or 1-4 lesions) from kidney cancer receive stereotactic radiosurgery (SRS) of fractionated stereotactic radiotherapy (FSRT) (3-6). The majority of kidney cancer patients with multiple (mainly defined as >3 or >4 lesions) cerebral metastases receive whole-brain irradiation (WBI) (7-9). For patients with kidney cancer, WBI-doses higher than 30 Gy were reported to result in better survival and local (intracerebral) control than 10×3 Gy (10). Of the patients with cerebral metastases from kidney cancer, about 25% are aged ≥65 years (elderly patients) (3-10). Since these patients often have poor performance scores and significant comorbidities, they may not be able to sufficiently tolerate intensive local therapies such as SRS and FSRT or WBI with higher biologically effective doses. Some benefits of local therapies and higher-dose WBI in terms of less late toxicity and improved local control are more of an issue in patients with favorable survival prognoses (1, 3-10). Moreover, patients with a poor survival are better treated with short-course WBI to keep the time spent receiving anticancer treatment to a minimum (11). Therefore, it is important to estimate a patient's lifespan before assigning a treatment program. This study aimed to provide an instrument that can assist physicians in estimating the survival prognosis of elderly patients with cerebral metastases from kidney cancer.

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Key Words: Kidney cancer, cerebral metastases, elderly patients, radiotherapy, scoring instrument, survival prognosis.

Patients and Methods

A total of 24 elderly patients (65 years or older) with kidney cancer, who had developed cerebral metastases, were included in this retrospective study. The data of some of these patients were obtained from an existing database partly used for previous studies (8-12). The current study received approval from the Ethics Committee of the University of Lübeck (reference 19-011A). All 24 patients were treated with WBI alone, either with 5×4 Gy (1 week), 10×3 Gy (2 weeks) or total doses >30 Gy (doses per fraction of 2-3 Gy, 3-4 weeks). The WBI-regimen and six pre-treatment factors (Table I) were evaluated for associations with survival. These factors included age (≤70 *vs.* ≥71 years), gender, performance status (Karnofsky performance score (KPS) of <70 *vs.* ≥70), number of cerebral metastases (limited, 1-3 lesions *vs.* multiple, >3 lesions), extracranial metastases at the start of WBI (no *vs.* yes), and the time from kidney cancer diagnosis to WBI (<24 *vs.* ≥24 months).

For survival analyses, we used the Kaplan–Meier method supplemented by the log-rank test. The scoring instrument for estimation of survival was based on the factors showing a trend

Table I. *Summary of the factors analyzed for potential associations with survival.*

Factor	Number of patients (%)
Radiation regimen	
5×4 Gy	4 (16.7)
10×3 Gy	12 (50.0)
>30 Gy (2-3 Gy per fraction)	8 (33.3)
Age	
≤75 Years	9 (37.5)
≥76 Years	15 (62.5)
Gender	
Female	9 (37.5)
Male	15 (62.5))
Karnofsky performance score	
<60	11 (45.8)
≥70	13 (54.2)
Number of cerebral metastases	
Limited (1-3)	7 (29.2)
Multiple (>3)	17 (70.8)
Extra-cranial metastases at the start of WBI	
No	9 (37.5)
Yes	15 (62.5)
Time from kidney cancer diagnosis to WBI	
<24 Months	8 (33.3)
≥24 Months	16 (66.7)

WBI: Whole-brain irradiation.

Table II. *Survival rates at 3 and 6 months following WBI (univariate analyses).*

	At 3 months (%)	At 6 months (%)	*p*-Value
Radiation regimen			
5×4 Gy	75	50	0.226
10×3 Gy	42	17	
>30 Gy (2-3 Gy per fraction)	25	13	
Age			
≤75 Years	44	22	0.831
≥76 Years	40	20	
Gender			
Female	33	22	0.829
Male	47	20	
Karnofsky performance score			
<60	45	9	0.521
≥70	38	31	
Number of cerebral metastases			
Limited (1-3)	57	43	0.194
Multiple (>3)	35	12	
Extra-cranial metastases at the start of WBI			
No	33	22	0.902
Yes	47	20	
Time from kidney cancer diagnosis to WBI			
<24 Months	38	0	0.107
≥24 Months	44	31	

WBI: Whole-brain irradiation.

($p<0.20$) with respect to survival. For each factor included in the scoring instrument, 0 points (less favorable survival) and 1 point (more favorable survival) were awarded. The points of the factors were added for each patient to receive the so-called patient score.

Results

The median survival time following WBI in all 24 patients was 3 months, and the post-WBI 3-month and 6-month survival rates were 42% and 21%, respectively.

Two of the factors, namely number of cerebral metastases ($p=0.194$) and the time from kidney cancer diagnosis to WBI ($p=0.107$), showed a trend for an association with survival and were, therefore, included in the scoring instrument (Table II). The

The following factor points were assigned: 1-3 cerebral metastases=1 point, >3 cerebral metastases=0 points, time from kidney cancer diagnosis to WBI ≥24 months=1 point, and time from kidney cancer diagnosis to WBI <24 months=0 points. Thus, patient scores of 0, 1 and 2 points were produced. The corresponding 3-month survival rates were 33%, 38% and 60%, respectively, and the corresponding 6-month survival rates were 0%, 15% and 60%, respectively ($p=0.131$). Based on these survival rates, two prognostic groups were designed, namely 0-1 points (n=19) and 2 points (n=5). The survival rates of these two groups were 37% and 60%, respectively, at 3 months, and 11% and 60%, respectively, at 6 months ($p=0.108$, Figure 1).

Discussion

The prognoses of many patients with metastatic kidney cancer are poor. However, due to the recent introduction of novel systemic agents such as checkpoint inhibitors, patients with extracranial metastatic disease live longer (13-15). This likely has an impact on the risk of developing cerebral metastases, which increases with lifetime. Of the entire group of patients with cerebral metastases from kidney cancer, a considerable proportion was elderly. These patients should be analyzed separately due to significant comorbidities and reduced reserve. Many of these patients may be unable to withstand aggressive treatment regimens. Therefore, they likely will benefit from personalized treatment approaches that consider among other aspects a patient's survival prognosis. In general, patients with poor prognoses assigned to WBI should receive a WBI-regimen with a short overall treatment time, *e.g.* 5×4 Gy given in 1 week. In a previous retrospective study including patients

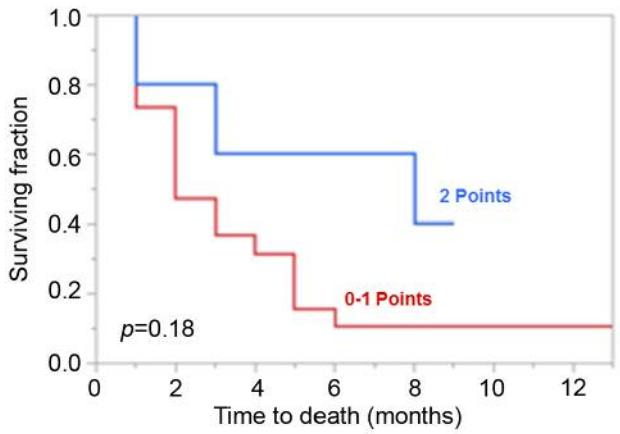

Figure 1. *Kaplan–Meier curves for survival of the two prognostic groups, 0-1 and 2 points.*

with poor prognoses and cerebral metastases of any age and with different primary tumor types, 5×4 Gy (n=232) was not associated with worse outcomes than 10×3 Gy in 2 weeks (n=210) in terms of local control (p=0.07) and survival (p=0.29) (11). Moreover, the rates of grade 3 acute toxicities were also not significantly different. On the contrary, patients with favorable survival prognoses may benefit from WBI with higher total doses and lower dose per fraction (16, 17). In longer-term survivors receiving WBI for cerebral metastases, total doses >30 Gy resulted in better local control and survival. One-year local control rates were 28% after 10×3 Gy and 44% after 20×2 Gy (p=0.047 on multivariate analysis), and 1-year survival rates were 50% and 61%, respectively (p=0.008 on multivariate analysis) (16). Moreover, WBI with doses per fraction of <3.0 Gy were reported to result in less prominent neuro-cognitive dysfunction when compared to ≥3.0 Gy (17). Thus, when aiming to assign the optimal WBI-regimen to a patient, it is important to estimate a patient's remaining lifespan. To achieve this goal, physicians can use scoring instruments (survival scores) that are available for several primary tumor types (18-20). In this study, a specific instrument for elderly kidney cancer patients has been created. This new instrument includes two prognostic groups, 0-1 and 2 points, with a remarkable difference regarding the 6-month survival probability. The 6-month survival rate of the patients in the 0-1 points group was only 11%. Therefore, these patients appear good candidates for WBI with 5×4 Gy in 1 week. Those patients achieving 2 points had a 6-month survival rate of 60%. Thus, these patients should receive longer-course WBI with higher total doses and lower doses per fraction (16, 17). According to a previous study of 60 patients treated with WBI for cerebral metastases from kidney cancer, WBI with total doses >30 Gy when compared to 10×3 Gy was associated with better 6-month survival (52% *vs*. 29%, p=0.003) and 6-month local control (57% *vs*. 21%, p=0.013) (10). Therefore, patients of the present study achieving 2 points should be considered for WBI with total doses >30 Gy. These patients with a better expected survival made up only 21% of the present study. When using these recommendations, the limitations of this study (retrospective design and small sample size), should be considered. In summary, this new instrument can assist physicians aiming to estimate a patient's survival prognosis prior to developing a personalized treatment program.

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

D.R., T.N. and S.E.S participated in the design of the study. T.N. and D.R. provided the data. Analyses of the data were performed by S.E.S. and D.R. S.E.S and D.R. The article was drafted by D.R. and S.E.S., and reviewed and approved by all Authors.

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