Estimation of the Six-month Survival Probability After Radiosurgery for Brain Metastases from Kidney Cancer

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Abstract. *Aim: To generate an overall survival score for patients with kidney cancer who underwent radiosurgery for brain metastases. Patients and Methods: Thirty-six patients who received radiosurgery alone for 1-3 brain metastases from kidney cancer were included. On multivariate analysis of a preceding study of such patients, Karnofsky performance score (KPS) and extracranial spread were significantly associated with overall survival and formed the basis for this score. For each patient, the prognostic score was derived from adding the points of KPS and extracranial spread resulting in a score of 9, 12, 15 or 18 points. Results: Six-month overall survival rates were 13% for patients with 9 points, 80% for those with 12 points, 79% for those with 15 points and 100% for those with 18 points, respectively. Three groups of patients were defined with scores of 9, 12-15 and 18 points. Six-month overall survival rates were 13%, 79% and 100%, respectively (p=0.004). Conclusion: This new score facilitates personalized treatment decisions for patients with kidney cancer with very few brain metastases.*

Kidney cancer is considered a relatively radioresistant tumor entity (1, 2). This therapeutic disadvantage can be compensated for with the use of higher radiation doses per treatment session (*i.e.* fraction). The administration of very high doses per fraction can be realized with high-precision techniques such as radiosurgery (2). Therefore, many patients with kidney cancer with a very limited number of brain metastases receive high-dose single-fraction radiosurgery, either alone or preceded by whole-brain irradiation (4, 5).

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Although the systemic treatment of kidney cancer has been improved during recent years, the benefits of new agents often do not reach cerebral lesions because most anticancer drugs do not pass the blood–brain barrier (6-8). Therefore radiotherapy including radiosurgery is very important for a successful treatment of brain metastases from kidney cancer. When the treating physicians are designing a personalized treatment concept in order to achieve the best results according to an individual patient's needs, it is considered mandatory to be able to know the patient's overall survival time as precisely as possible. This applies in particular for patients with metastatic disease such as brain metastasis. Therefore, overall survival scores are desirable. In the present study, an overall survival score has been generated particularly for patients with kidney cancer treated with radiosurgery for very few brain metastases. In order to minimize the risk of a treatment-related selection bias, solely patients who received radiosurgery alone (*i.e.* without whole-brain irradiation) were included.

Patients and Methods

A total of 36 patients who received single-fraction radiosurgery alone with 16-23 Gy for a very limited number of brain metastases from kidney cancer (renal cell carcinoma) were included in this retrospective multicenter study. The characteristics of these 36 patients are given in Table I. In the multivariate analysis of a preceding study of such patients, the Karnofsky performance score (KPS 60-70 *vs.* KPS 80-100) and the presence of extracranial metastatic disease (no *vs.* yes) were significantly associated with overall survival after the radiosurgery treatment (9). In that study, the six-month rates of overall survival were 25% in patients with a KPS of 60-70, and 90% in patients with a KPS of 80-100; 59% in patients with extracranial spread and 91% in patients without extracranial spread.

In the present study, an instrument was designed to enable the treating physicians to pre-estimate the overall survival prognosis of a patient presenting with brain metastases from kidney cancer. The above mentioned six-month overall survival rates of the preceding study formed the basis for this instrument (9). The six-month overall

survival rates of the preceding study were divided by 10 resulting in 3 points for those with KPS of 60-70, 9 points for those with KPS of 80-100, 6 points for patients with extracranial spread, and 9 points for patients without extracranial spread (9). For each patient, the prognostic score was derived from the addition of the points for the two significant factors KPS and extracranial spread, resulting in possible scores of 9 points, 12 points, 15 points or 18 points. The six-month and 12-month overall survival rates for patients in each of the four score groups were determined with a Kaplan–Meier analysis.

Results

The six-month overall survival rates for patients with scores of 9 (n=8), 12 (n=5), 15 (n=14) and 18 points (n=9) were 13%, 80%, 79% and 100%, respectively, and the corresponding 12-month overall survival rates were 13%, 27%, 53% and 70%, respectively. According to the overall survival rates, the following three groups were defined for patients with: 9 points (n=8), 12-15 points (n=19) and 18 points (n=9). The six-month overall survival rates for these groups were 13%, 79% and 100%, respectively, and the 12-month overall survival rates were 13%, 46% and 70%, respectively (p=0.004 for overall comparison of the three groups). The p-value for the comparison of the groups with 9 points and 12-15 points was 0.016, and the p-value for the comparison of the groups with 12-15 points and 18 points was 0.53.

Table I. *Characteristics of the 36 patients included in this study.*

	Number of patients (n)	Proportion of patients (%)
Age		
≤65 years	20	56
>65 years	16	44
Gender		
Female	9	25
Male	27	75
Karnofsky performance score		
60-70	13	36
80-100	23	64
Number of brain metastases		
1	20	56
2-Mαϱ	16	44
Extracranial spread		
No	14	39
Yes	22	61
Interval from diagnosis of kidney cancer to radiosurgery (median value: 18 months)		
≤18 months	18	50
>18 months	18	50

Discussion

An improvement regarding the control of locoregional disease in patients with cancer leads to longer overall survival. Since the risk of experiencing metastatic spread increases with a patient's lifetime, improved locoregional control would likely result in a greater number of patients needing treatment for metastatic disease. This also applies to patients with kidney cancer (6-8). Many patients who present with metastatic kidney cancer, such as with brain metastases, need a personalized treatment approach to avoid under- or over-treatment. Patients with very few cerebral lesions appear to be good candidates for radiosurgery with or without whole-brain irradiation (4, 5). In order deliver a personalized radiation treatment, one needs to know an individual patient's overall survival time as precisely as possible. Prognostic factors and prognostic scores contribute to such knowledge. Prognostic factors may include both pre-clinical and clinical factors. For example, vascular endothelial growth factor has been described as a marker or regulator of the aggressiveness of kidney cancer (10, 11). The TNM-C score, which combines the TNM stage and C-reactive protein level, has also been shown to be of predictive value for patients with kidney cancer (12). In our own preceding study of patients with kidney cancer who were treated with radiosurgery for brain metastases, the performance status (namely KPS) and the presence or not of extracranial metastatic disease proved to be independent predictors of overall survival for such patients (9).

To be even better able to tailor the treatment regimen to a single patient, a survival score was generated in the current study considering both KPS and extracranial metastatic disease. This new score was designed for patients with 1-3 brain metastases and used to form three prognostic groups. Only 13% of the patients who achieved only 9 points survived six months or longer following radiosurgery alone. In 88% of these patients, the cause of death was extracranial spread. Therefore, a major focus for patients with 9 points should be on palliative systemic treatment, whereas the addition of whole-brain irradiation appears to be not important. Patients who achieved 12-15 points had an intermediate overall survival prognosis; the main causes of death were either new brain metastases or systemic progression. Therefore, these patients may benefit from both additional whole-brain irradiation and early systemic treatment. Those patients achieving 18 points had a very favorable survival prognosis, with overall survival rates of 100% at six months and 70% at 12 months, respectively. The major cause of death was a recurrence of the brain metastases treated with radiosurgery alone. Since the

addition of whole-brain irradiation may be associated with neurocognitive deficits and most patients with 18 points live long enough to experience such deficits, whole-brain irradiation might not be added to radiosurgery during primary treatment of brain metastases but spared as an option for salvage treatment (13).

In summary, in the present study, a new survival score was created for patients with 1-3 brain metastases from kidney cancer who received radiosurgery alone. Three prognostic groups were formed which make it easier for the treating physicians to choose the best personalized approach for a patient in their particular situation.

Conflicts of Interest

The Authors state that there is no conflict of interest related to this study.

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