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Predicting Survival After Irradiation for Brain Metastases from Head and Neck Cancer

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Abstract. *Aim: Patients with cerebral metastases from head and neck cancer are not common. This study aimed to create an instrument for estimating survival in this particular group of patients. Patients and Methods: Survival was significantly influenced by Eastern Cooperative Oncology Group (ECOG) performance score, number of cerebral lesions and extracranial metastatic disease. These characteristics were included in our score. Results: Scoring was based on 6-month survival data: ECOG 0-1=1 point, ECOG 2-3=0 points, 1-3 cerebral lesions=1 point, ≥4 cerebral lesions=0 points, lack of extracranial metastases=1 point, and presence of extracranial metastases=0 points. Addition of these points for each patient resulted in 0-3 points. Three groups were built comprising 0-1, 2 and 3 points. Six-month survival rates for these groups were 0%, 50% and 100%, respectively. Conclusion: This new instrument guides physicians in choosing optimal irradiation programs for patients with cerebral metastases from head-and-neck cancer.*

Patients with locally advanced head and neck cancer have a poor prognosis, which applies particularly to patients with metastatic disease including brain metastases (1). Because patients with head and neck cancer represent a small group of patients with cerebral metastases, the optimal treatment approach for individual patients is often not properly defined for this sub-group. Treatment decision processes could be facilitated with an instrument that allows treating physicians to estimate the patient's life expectancy. Knowledge of the remaining lifetime will affect the selection of appropriate regimen, including local treatments such as neurosurgery or radiosurgery, as well as whole-brain irradiation (WBI) programs (2, 3). Such knowledge can be gained from predictive tools. Because primary tumors, particularly in a metastasized situation, are different with respect to tumor biology, metastatic pattern, and prognosis in general, each primary tumor type requires its own prognostic instrument (4, 5). The current study was performed to create such an instrument specifically for patients with cerebral metastases from head and neck cancer.

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Patients and Methods

In this study, the data of 25 patients treated with WBI for cerebral metastases from head-and-neck cancer between 2000 and 2014 were analyzed. The WBI dose (4 Gy ×5 *versus* 3 Gy ×10 *versus* 2 Gy ×20) plus the following seven additional characteristics were analyzed for associations with post-WBI survival: age (≤64 *versus* ≥65 years, median age=64 years), gender, Eastern Cooperative Oncology Group (ECOG) performance score (0-1 *versus* 2-3), primary tumor site (nasopharynx *versus* oropharynx *versus* hypopharynx *versus* larynx *versus* parotid glands *versus* oral cavity/floor of mouth), time between first diagnosis of head-and-neck cancer and WBI (≤24 *versus* ≥25 months, median time=24 months), number of cerebral lesions (1-3 *versus* ≥4 lesions), and the presence of extracranial metastases (no *versus* yes). The distributions of all eight characteristics are shown in Table I.

The survival analysis was performed with the Kaplan–Meier method, and the *p*-values were obtained from the log-rank test. The characteristics which achieved significance were included in the predictive instrument. For each significant characteristic, a score of 0 (unfavorable survival prognosis) or 1 (favorable survival prognosis) was given. The prognostic score for each patient was calculated by adding the scores for the significant prognostic factors.

Table I. *Patients' characteristics.*

	Patients N	Proportion %
Age		
≤64 years	13	52
≥65 years	12	48
Gender		
Female	8	32
Male	17	68
ECOG performance score		
0-1	11	44
2-3	14	56
Tumor site		
Nasopharynx	3	12
Oropharynx	5	20
Hypopharynx	3	12
Larynx	5	20
Parotid glands	4	16
Oral cavity/floor of mouth	5	20
Time from cancer diagnosis to WBI		
≤24 months	13	52
≥25 months	12	48
Number of cerebral metastases		
1-3	11	44
≥4	14	56
Extracranial metastases		
No	9	36
Yes	16	64
WBI program		
4 Gy ×5	5	20
3 Gy ×10	16	64
2 Gy ×20	4	16

ECOG: Eastern Cooperative Oncology Group; WBI: whole-brain irradiation.

Table II. *Characteristics and corresponding survival rates at six and 12 months.*

	Survival at 6 months (%)	Survival at 12 months (%)	*p*-Value
Age			
≤64 years	33	17	
≥65 years	20	10	0.68
Gender			
Female	43	14	
Male	20	13	0.90
ECOG performance score			
0-1	75	38	
2-3	0	0	<0.001
Tumor site			
Nasopharynx	0	0	
Oropharynx	25	0	
Hypopharynx	0	0	
Larynx	67	33	
Parotid glands	25	25	
Oral cavity/floor of mouth	40	14	0.16
Time from cancer diagnosis to WBI			
≤24 months	23	8	
≥25 months	33	22	0.23
Number of cerebral metastases			
1-3	75	38	
≥4	0	0	<0.001
Extracranial metastases			
No	83	50	
Yes	6	0	0.002
WBI schedule			
4 Gy ×5	0	0	
3 Gy ×10	21	7	
2 Gy ×20	75	50	0.12

ECOG: Eastern Cooperative Oncology Group; WBI: whole-brain irradiation.

Results

In the survival analysis, three of the investigated characteristics, namely ECOG performance score, number of cerebral lesions and presence of extracranial metastases, had a significant impact on survival. The results of the analysis of survival are given in Table II. The scores obtained for the three characteristics found to be significantly associated with survival were as follows: ECOG 0-1=1 point, ECOG 2-3=0 points, 1-3 cerebral lesions=1 point, ≥4 cerebral lesions=0 points, lack of extracranial metastases=1 point and presence of extracranial metastases=0 points. The addition of the scores of the three characteristics resulted in prognostic scores of 0 to 3 points (n=12, n=3, n=2 and n=8 for scores of 0, 1, 2 and 3, respectively). The 6-month survival rates related to these scores were 0%, 0%, 50% and 100%, respectively (p=0.002). Based on these scores, the following three survival groups were built: 0-1 points, 2 points and 3 points. The corresponding 6-month survival rates were 0%, 50% and 100%, respectively. The corresponding 12-month survival rates were 0%, 0% and 63%, respectively.

Discussion

In order to improve the prognosis of patients with head-and-neck cancer, considerable efforts have been made in recent years, for example by introducing new anticancer therapies (6-8). Another approach for improving the treatment results is the individualization of therapeutic approaches by including prognostic factors into treatment decisions (9-13). Knowing a patient's survival time is a very important aspect with respect to optimal individualization of their treatment. This applies particularly to patients with metastatic disease. Patients with brain metastases require particular attention, since many of these patients develop serious symptoms such as seizures, visual disorders, signs of paralysis and character changes (1).

Therefore, survival tools have been developed for these patients in general and, in addition, specifically for single tumor entities (5, 14-17). However, a specific score for patients with cerebral metastases from head-and-neck cancers has been lacking.

In the present study, such a score was created. Three significant prognostic factors were identified: ECOG performance score, number of cerebral lesions and presence of extracranial metastatic disease. Our new predictive instrument was based on these three characteristics and allowed the building of three groups with 6-month survival rates of 0% (0-1 points), 50% (2 points) and 100% (3 points). Since the prognosis of patients with 0-1 points is extremely poor, these patients should ideally receive a short WBI program such as 4 Gy ×5 in one week to avoid spending more time than necessary receiving treatment. This recommendation is supported by a study of patients with cerebral metastases from different tumor entities that reported similar survival rates after 4 Gy ×5 and after 3 Gy ×10 (24% and 27%, respectively; p=0.29) (18). In the group of patients with only 0-1 points, even best supportive care alone may be an option. Patients who achieve 2 points are suitable candidates for the most commonly used WBI program worldwide of 3 Gy ×10 (1). Patients with 3 points have a much more favorable survival prognosis and could benefit from a WBI program with a total dose of greater than 30 Gy and a dose per fraction of less than 3 Gy (19, 20). A total dose beyond 30 Gy was reported to result in improved 1-year intracerebral control rates (44% *vs*. 28%, p=0.06) and improved 1-year survival rates (61% *vs*. 50%) when compared to 3 Gy ×10 (19). Furthermore, doses per fraction of less than 3 Gy are associated with less neurocognitive decline than doses of ≥3 Gy (20). Patients with 3 points and a limited number of cerebral lesions might also be considered for more intensive local treatment, including resection, radiosurgery or fractionated stereotactic radiotherapy (2, 3).

In conclusion, this new score for patients with cerebral metastases from head-and-neck cancer contributes to the selection of optimal personalized treatment approaches.

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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