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Predictive Factors and a Survival Score for Patients Irradiated for Metastatic Spinal Cord Compression from Carcinoma of the Salivary Glands

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Abstract. *Aim: To our knowledge, this is the first study focusing on metastatic spinal cord compression (MSCC) from carcinoma of the salivary glands. Patients and Methods: Nine patients receiving radiation alone were evaluated for improvement of motor deficits, post-radiation gait function and survival. Results: Of nine characteristics (radiation program, age, sex, additional metastases to bone or to other organs, dynamic of motor deficits, pre-radiation gait function, number of vertebrae affected by MSCC, general condition), strong trends were found for associations between improved motor deficits and their dynamic (p=0.05), post-radiation gait function and pre-treatment ambulatory status (p=0.08) and between survival and additional metastases to other organs (p=0.07), dynamic of motor deficits (p=0.07) and general condition (p=0.07). In addition, a survival score was created. Patients with 2-3 points had a significantly better 6-month survival than those with 0-1 points (100% vs. 0%, p=0.027). Conclusion: Characteristics predicting outcomes identified in this study and the new survival score can guide physicians when making treatment decisions.*

Due to modern treatment approaches, patients with cancer nowadays live longer than a few decades before and, therefore, bear a higher risk of experiencing the development of distant metastases during the course of their disease (1). This also applies to bone metastases. About 50% of bone metastases occur in the vertebral column, and in up to 10% of adult patients with cancer, vertebral metastases lead to spinal cord compression (MSCC) (2). MSCC, if not treated, generally results in progressive motor deficits and finally in complete paraplegia. The most common treatment regimen for MSCC worldwide consists of radiation alone (2). For the radiation treatment of MSCC, several dose-fractionation programs are available that range from a single treatment session with a high dose per fraction (for example 8 Gy or 10 Gy) to longer-lasting programs with higher total doses of 30-40 Gy and lower doses per fraction of 2-3 Gy that are given over 2-4 weeks (3). In addition, shorter-course programs such as 5×4 Gy given over 1 week are widely used. Taking into account the available data from both prospective and large retrospective studies, patients with a poor survival prognosis should be treated with single-fraction or shorter-course radiation programs, whereas those patients with a more favorable survival prognosis can benefit from longer-lasting programs in terms of better local control and survival and less late treatment-related morbidity (4-8). Therefore, studies aiming to identify prognostic factors and to develop survival scores have been performed for patients with MSCC in general and for patients with MSCC from specific tumor entities (9-16). In order to provide the best possible radiation treatment for an individual patient, studies focusing on a specific tumor type are important, because tumor entities leading to MSCC vary considerably regarding their biology and patterns of metastatic spread (9, 12, 14-16). Therefore, the current study was conducted focusing particularly on patients with MSCC from carcinoma of the salivary glands. Since such patients are very rare and account for fewer than 0.5% of patients with MSCC, to our knowledge, this is the first study reported so far that investigated the outcomes after radiation in this group of patients.

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Patients and Methods

This retrospective study was based on the data of nine patients treated with radiation alone for MSCC from carcinoma of the salivary glands. In this cohort, nine characteristics were investigated with respect to the improvement rate of motor deficits, post-radiation gait function and the 6-month survival rate. The

Table I. *Patient characteristics*.

Characteristic	Number of patients
Radiation program	
5×4 Gy	2
10×3 Gy/20×2 Gy	7
Age	
<60 Years	6
≥60 Years	3
Gender	
Female	1
Male	8
Additional metastasis to bone	
No	4
Yes	5
Additional metastasis to other organs	
No	5
Yes	4
Dynamic of motor deficits	
Fast (1-14 days)	6
Slow (>14 days)	3
Pre-radiation gait function	
Ambulatory	6
Not ambulatory	3
Number of affected vertebrae	
1-3	4
≥4	5
General condition	
ECOG PS 2	5
ECOG PS 3-4	4

ECOG PS: Eastern Cooperative Oncology Group performance score.

Table II. *Analysis of improvement of motor deficits following radiation*.

Factor	Improvement of motor deficits, n (%)	*p*-Value
Radiation program		
5×4 Gy (N=2)	0 (0)	
10×3 Gy/20×2 Gy (N=7)	2 (29)	0.48
Age		
<60 Years (n=6)	2 (33)	
≥60 Years (n=3)	0 (0)	0.30
Gender		
Female (N=1)	0 (0)	
Male (N=8)	2 (25)	0.64
Additional metastasis to bone		
No (N=4)	1 (25)	
Yes (N=5)	1 (20)	0.87
Additional metastasis to other organs		
No (N=5)	2 (40)	
Yes (N=4)	0 (0)	0.20
Dynamic of motor deficits		
Fast (1-14 days) (N=6)	0 (0)	
Slow (>14 days) (N=3)	2 (67)	0.05
Pre-radiation gait function		
Ambulatory (N=6)	2 (33)	
Not ambulatory (N=3)	0 (0)	0.30
Number of affected vertebrae		
1-3 (N=4)	1 (25)	
≥4 (N=5)	1 (20)	0.87
General condition		
ECOG PS 2 (N=5)	2 (40)	
ECOG PS 3-4 (N=4)	0 (0)	0.20
Entire cohort (N=9)	2 (22)	

ECOG PS: Eastern Cooperative Oncology Group performance score.

characteristics are summarized in Table I and comprised the type of radiation program, age, sex, additional metastases to bone or other organs, the dynamic of the development of motor deficits, pre-radiation gait function, the number of vertebrae affected by MSCC and the patients' general condition measured with the Eastern Cooperative Oncology Group performance score (ECOG PS). The analyses with respect to the three endpoints were performed with the chi-square test. Results were rated as being significant when the *p*-value was less than 0.05. A strong trend was considered to list when the *p*-value was 0.05-0.08. Those characteristics showing at least a strong trend for an association with survival were incorporated into a survival score.

Results

In the analyses performed regarding the improvement of motor deficits by radiation therapy, the dynamic of the development of motor deficits showed a strong trend and was almost significant (p=0.05). A slower development (>14 days) was associated with more favorable outcomes than a faster dynamic (1-14 days) (Table II). With respect to post-radiation gait function, the ambulation status prior to radiation showed a strong trend (p=0.08). All patients who were initially able to walk maintained this ability, whereas no patient who was unable to walk prior to radiation regained ambulatory status following treatment (Table III). On survival analyses, three characteristics showed a strong trend for an association with outcomes. Improved 6-month survival was found in the case of no additional metastasis to other organs (p=0.07), slower (>14 days) development of motor deficits (p=0.07) and better general condition (ECOG PS of 2) prior to radiation (p=0.07) (Table IV).

These three characteristics were included in a survival score designed for estimation of the 6-month survival probability. The following points were assigned to these characteristics: No additional metastasis to other organs=0 points, additional metastasis to other organs=1 point; slow (>14 days) development of motor deficits=0 points, fast (1-14 days) development of motor deficits=1 point; ECOG PS 2=0 points, ECOG PS 3-4=1 point. Total scores ranged from 0 to 3 points. Six-month survival rates were 0% (0/3 patients) for those with 0 points, 0% (0/2) for those with 1

Table III. *Analysis of post-radiation gait function.*

Factor	Ambulatory post-radiation, n (%)	*p*-Value
Radiation program		
5×4 Gy (N=2)	1 (50)	
10×3 Gy/20×2 Gy (N=7)	5 (71)	0.77
Age		
<60 Years (n=6)	4 (67)	
≥60 Years (n=3)	2 (67)	1.00
Gender		
Female (N=1)	0 (0)	
Male (N=8)	6 (75)	0.37
Additional metastasis to bone		
No (N=4)	3 (75)	
Yes (N=5)	3 (60)	0.81
Additional metastasis to other organs		
No (N=5)	4 (80)	
Yes (N=4)	2 (50)	0.57
Dynamic of motor deficits		
Fast (1-14 days) (N=6)	3 (50)	
Slow (>14 days) (N=3)	3 (100)	0.39
Pre-radiation gait function		
Ambulatory (N=6)	6 (100)	
Not ambulatory (N=3)	0 (0)	0.08
Number of affected vertebrae		
1-3 (N=4)	3 (75)	
≥4 (N=5)	3 (60)	0.81
General condition		
ECOG PS 2 (N=5)	4 (80)	
ECOG PS 3-4 (N=4)	2 (50)	0.57
Entire cohort (N=9)	6 (67)	

ECOG PS: Eastern Cooperative Oncology Group performance score.

Table IV. *Analysis of survival at 6 months following radiation.*

Factor	Survival a 6 months, n (%)	*p*-Value
Radiation program		
5×4 Gy (N=2)	1 (50)	
10×3 Gy/20×2 Gy (N=7)	3 (43)	0.90
Age		
<60 Years (n=6)	3 (50)	
≥60 Years (n=3)	1 (33)	0.75
Gender		
Female (N=1)	0 (0)	
Male (N=8)	4 (50)	0.50
Additional metastasis to bone		
No (N=4)	2 (50)	
Yes (N=5)	2 (40)	0.84
Additional metastasis to other organs		
No (N=5)	4 (80)	
Yes (N=4)	0 (0)	0.07
Dynamic of motor deficits		
Fast (1-14 days) (N=6)	1 (17)	
Slow (>14 days) (N=3)	3 (100)	0.07
Pre-radiation gait function		
Ambulatory (N=6)	4 (67)	
Not ambulatory (N=3)	0 (0)	0.17
Number of affected vertebrae		
1-3 (N=4)	2 (50)	
≥4 (N=5)	2 (40)	0.84
General condition		
ECOG PS 2 (N=5)	4 (80)	
ECOG PS 3-4 (N=4)	0 (0)	0.07
Entire cohort (N=9)	44	

ECOG PS: Eastern Cooperative Oncology Group performance score.

point, 100% (1/1) for those with 2 points and 100% (3/3) for those with 3 points. Based on the 6-month survival rates, two groups were formed, with 0-1 and 2-3 points. Six-month survival rates were 0% and 100%, respectively (p=0.027).

Discussion

Tumors of the salivary glands are rare and account for only 3-10% of all head-and-neck tumors (17-20). About one-third of these tumors are malignant (19, 20). Most studies reporting on malignant salivary gland tumors have been performed in patients undergoing local treatment for non-metastatic disease (17, 20, 21). Less data are available for patients with metastatic salivary gland carcinoma, who generally have a poor prognosis despite the availability of modern anticancer treatments (1, 22). Outcomes of these patients may be improved with personalization of their treatment taking into account an individual patient's survival prognosis. Personalization of the treatment can be facilitated with knowledge of prognostic factors and, ideally, with the availability of scoring tools that allow an estimation of the patient's remaining lifetime. The present study focused on MSCC in patients with carcinoma of the salivary glands and aimed to identify prognostic factors for treatment outcomes and to develop a specific survival score for these patients. Predictors of outcomes and survival scores are already available for patients with MSCC from other primary tumor types (9-16, 23, 24).

In the present study, improvement of motor deficits by radiation was associated with the dynamic of the development of motor deficits prior to the start of treatment. A slower development was associated with a better functional outcome, which has been described before in other series of patients with MSCC (3, 5, 25). These results can be explained by the fact that a slower compression of the spinal cord mostly affects the veins and is reversible after radiation. In contrast, a rapid development of motor deficits is mostly due to compression of the spinal arteries, which can result in non-reversible spinal cord infarction (25). In the current study, post-radiation ambulatory status was associated with pre-radiation gait function. The fact that

patients who are able to walk often maintain this ability, whereas patients unable to walk often do not regain their walking ability, has already been described in previous studies (26-28). This demonstrates the results of the present study are consistent with those of the available literature.

In this study, improved 6-month survival was associated with absence of additional metastasis to other organs, slower development of motor deficits prior to the start of radiation and a better general condition prior to radiation. These factors were also described for patients with MSCC from some other primary tumor types, also demonstrating concordance of the results of the present study with those of other studies (9-16, 23, 24). The fact that these three characteristics were not associated with survival in patients with MSCC from all other primary tumors supports the idea that primary tumors associated with MSCC vary regarding their biological behavior (2).

Based on the three characteristics additional metastases to other organs, dynamic of the development of motor deficits and the patients' general condition, a survival score was created in order to predict the 6-month survival probability of patients with MSCC from carcinoma of the salivary glands. Two prognostic groups were identified with significantly different 6-month survival rates, those with 0-1 points and those with 2-3 points. No patient of the 0-1 point group survived 6 months or longer, and the median survival time was only 4 months. Therefore, these patients should receive a short radiation program such as 1×8 Gy or 5×4 Gy in 1 week to avoid spending more of their remaining lifetime receiving treatment than necessary (2-8). In the group with 2-3 points, all patients lived for 6 months or longer (median survival time >8 months, not yet reached). Therefore, these patients can be considered good candidates for longer-course radiation programs such as 10×3 Gy over 2 weeks or 20×2 Gy over 4 weeks, since these programs provide better local control of MSCC than shorter regimens (2, 3, 8).

In conclusion, this study identified prognostic factors for improvement of motor deficits, post-treatment gait function and survival in patients irradiated for MSCC from salivary gland cancer. In addition, a survival score was developed that allows an estimation of the 6-month survival probability of such patients. Both prognostic factors and the score can help the physician to assign an appropriate radiation program to these patients and personalize their treatment approach.

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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