Predicting the Ambulatory Status of Patients Irradiated for Metastatic Spinal Cord Compression (MSCC) from Head-and-neck Cancer

DIRK RADES¹, CHRISTIAN STAACKMANN¹ and STEFAN JANSSEN^{1,2}

¹Department of Radiation Oncology, University of Lübeck, Lübeck, Germany;

²Private Practice of Radiation Oncology, Hannover, Germany

Abstract. *Background/Aim: Personalized cancer care can improve patient outcomes and is facilitated by scoring systems. This study aimed to create an instrument to estimate ambulatory status after radiotherapy for metastatic spinal cord compression (MSCC) from head-and-neck cancer. Patients and Methods: In 60 patients, fractionation regimen plus 10 pre-treatment factors were analyzed for post-treatment ambulatory status. Significant factors were used for the scoring system by dividing the ambulatory rate (in %) by 10. Patients' scores were received by adding the factor scores. Results: Time developing motor deficits >7 days ($p=0.011$), being ambulatory prior to radiotherapy ($p<0.001$) and ECOG performance score 1-2 ($p<0.001$) showed significant associations with post-treatment ambulatory status. Patients' scores were 7, 12, 15, 20, 22 and 27 points. Three groups were designed (7-12, 15-20 and 22-27 points) with post-treatment ambulatory rates of 11%, 62% and 96% ($p<0.001$). Conclusion: This scoring system helps predict ambulatory status after radiotherapy for MSCC from head-and-neck cancer.*

Metastatic spinal cord compression (MSCC) is generally associated with neurologic dysfunction mainly with motor deficits (1, 2). For these patients, maintaining or regaining the ability to walk, either with or without aid, is a very important endpoint. This may be achieved with radiotherapy alone, which still is the most frequent treatment for MSCC (3-5). In case of inadequate response to radiotherapy patients may not be able to walk after treatment and might have done

better with upfront decompressive surgery plus stabilization (6, 7). However, upfront surgery has been reported to be associated with severe complications in more than 10% of the patients and is generally reserved for selected patients with a good performance status and a relatively favorable survival prognosis (6-8). In order to assign the most appropriate treatment protocol to a patient with MSCC, it would be helpful to be able to estimate the patient's ambulatory status following radiotherapy alone. Since MSCC is considered an oncologic emergency and, therefore, treatment decisions have to be made fast, a simple scoring system would be of great value for clinicians that helps predict post-treatment ambulatory status following radiotherapy alone (1, 2).

It has been previously stated that it is reasonable to identify predictive factors and develop scoring systems specifically for single tumor entities associated with MSCC due to differences, for example, with respect to tumor biologies, patterns of metastatic spread and survival prognoses (9-15). Therefore, the present study aims to create a scoring system that supports clinicians to estimate the post-treatment ambulatory status of patients irradiated for MSCC, particularly for those patients with MSCC from head-and-neck cancer.

Patients and Methods

Sixty patients who had been treated with radiotherapy alone for motor deficits due to MSCC from head-and-neck cancer between 1997 and 2015 were retrospectively evaluated for ambulatory status at 1 month following irradiation. The fractionation regimen (short-course radiotherapy (1×8 Gy or 5×4 Gy) vs. 10×3 Gy vs. longer-course radiotherapy with total doses >30 Gy (15×2.5 Gy or 20×2 Gy)) plus 10 pre-treatment factors were analyzed. The pre-treatment factors included age (≤ 59 years vs. ≥ 60 years, median 59 years), interval between first diagnosis of head-and-neck cancer and radiotherapy of MSCC (≤ 15 months vs. >15 months (4, 16)), visceral metastasis (no vs. yes), other bone metastasis (no vs. yes), cancer site (nasopharynx vs. oropharynx vs. hypopharynx vs. larynx vs. other

Correspondence to: Dirk Rades, MD, Department of Radiation Oncology, University of Lübeck, Lübeck, Ratzeburger Allee 160, 23562 Lübeck, Germany. Tel: +49 45150045401, Fax: +49 45150045404, e-mail: Rades.Dirk@gmx.net

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sites), gender, time developing motor deficits (1-7 days *vs.* >7 days (17)), ambulatory status prior to radiotherapy (not ambulatory *vs.* ambulatory), number of vertebrae affected by MSCC, (1-2 *vs.* ≥ 3 , median 3), and performance score according to the Eastern Cooperative Oncology Group (ECOG) (1-2 *vs.* 3-4, median 3). Distributions of all 11 factors are summarized in Table I.

The statistical analyses regarding the post-treatment ambulatory status were performed with the Chi-square test. Factors that achieved significance ($p < 0.05$) were used for the scoring system developed to estimate the probability of being ambulatory at 1 month following irradiation. For each significant factor, a factor score was calculated by dividing the ambulatory rate in percent by 10. The individual score for each patient was received by adding the factor scores.

Results

Three of the investigated factors showed a significant positive association with the post-treatment ambulatory status, namely time developing motor deficits of >7 days ($p = 0.011$), being ambulatory prior to radiotherapy ($p < 0.001$), and an ECOG performance score 1-2 ($p < 0.001$). The post-treatment ambulatory rates of all investigated factors are summarized in Table II. The post-treatment ambulatory rates of the three significant factors were used to develop the scoring system (Table III). The individual scores for the 60 patients were 7 points, 12 points, 15 points, 20 points, 22 points and 27 points, respectively (Figure 1). Three prognostic groups were designed, namely 7-12 points (group A), 15-20 points (group B) and 22-27 points (group C), respectively. The corresponding post-treatment ambulatory rates at 1 month following radiotherapy were 11% for group A, 62% for group B and 96% for group C, respectively ($p < 0.001$). The p-values for the comparisons of groups A *vs.* B and B *vs.* C were 0.027 and 0.034, respectively. In group C, ambulatory rates at 3 months and at 6 months following radiotherapy were 100% (24 of 24 patients) and 100% (20 of 20 patients), respectively.

Discussion

The survival prognosis of patients with locally advanced head-and-neck cancer has been improved due to novel treatment approaches including surgery, radiotherapy and systemic therapies (18-20). Since the risk of developing distant metastasis increases with lifetime, the number of patients presenting with metastatic disease such as MSCC is growing. Radiotherapy alone is the most common treatment for MSCC (1, 2). In 2005, a randomized trial of 101 patients that compared radiotherapy alone to radiotherapy plus upfront decompressive surgery showed that selected patients (MSCC from a solid tumor, Karnofsky performance score of 70 or greater, survival prognosis of 3 months or longer, involvement of only one spinal segment by MSCC and paraplegia lasting for not longer than 48 h) could benefit from

Table I. Distributions of the evaluated factors.

	Number of patients (%)
Age at the time of irradiation	
≤59 years	33 (55)
≥60 years	27 (45)
Interval between cancer diagnosis and radiotherapy of MSCC	
≤15 months	25 (42)
>15 months	35 (58)
Visceral metastasis	
No	31 (52)
Yes	29 (48)
Other bone metastasis	
No	27 (45)
Yes	33 (55)
Cancer site	
Nasopharynx	8 (13)
Oropharynx	16 (27)
Hypopharynx	9 (15)
Larynx	11 (18)
Other sites	16 (27)
Gender	
Female	9 (15)
Male	51 (85)
Time developing motor deficits	
1-7 days	21 (35)
>7 days	39 (65)
Pre-treatment ambulatory status	
Not ambulatory	19 (32)
Ambulatory	41 (68)
Number of affected vertebrae	
1-2	28 (47)
≥3	32 (53)
ECOG performance score	
1-2	28 (47)
3-4	32 (53)
Fractionation regimen	
Short-course radiotherapy (1×8 Gy, 5×4 Gy)	14 (23)
10×3 Gy	25 (42)
Longer-course radiotherapy (total doses >30 Gy)	21 (35)

MSCC: Metastatic spinal cord compression; ECOG: Eastern Cooperative Oncology Group.

the addition of surgery with respect to post-treatment ambulatory status and survival (6). In general, these criteria are met by 10-15% of patients with MSCC. Insufficient response to radiotherapy is considered another good indication for decompressive surgery plus stabilization (1, 2). Therefore, it would be helpful to be able to predict the response prior to the start of treatment. From the patient's point of view, post-treatment ambulatory status is a major key point with respect to their quality of life. From the physician's point of view, it is very important to know prior to assigning a treatment to a patient whether the ability to walk can be

Table II. *Post-treatment ambulatory status.*

	Number of patients (%)		<i>p</i> -Value
	Ambulatory	Not ambulatory	
Age at the time of irradiation			
≤59 years	22 (67)	11 (33)	0.844
≥60 years	15 (56)	12 (44)	
Interval between cancer diagnosis and radiotherapy of MSCC			
≤15 months	12 (48)	13 (52)	0.340
>15 months	25 (71)	10 (29)	
Visceral metastasis			
No	23 (74)	8 (26)	0.231
Yes	14 (48)	15 (52)	
Other bone metastasis			
No	19 (70)	8 (30)	0.650
Yes	18 (55)	15 (45)	
Cancer site			
Nasopharynx	6 (75)	2 (25)	0.987
Oropharynx	9 (56)	7 (44)	
Hypopharynx	7 (78)	2 (22)	
Larynx	6 (55)	5 (45)	
Other sites	9 (56)	7 (44)	
Gender			
Female	6 (67)	3 (33)	0.987
Male	31 (61)	20 (39)	
Time developing motor deficits			
1-7 days	7 (33)	14 (67)	0.011
>7 days	30 (77)	9 (23)	
Pre-treatment ambulatory status			
Not ambulatory	2 (11)	17 (89)	<0.001
Ambulatory	35 (85)	6 (15)	
Number of affected vertebrae			
1-2	17 (61)	11 (39)	0.999
≥3	20 (63)	12 (37)	
ECOG performance score			
1-2	27 (96)	1 (4)	<0.001
3-4	10 (31)	22 (69)	
Fractionation regimen			
Short-course radiotherapy (1×8 Gy, 5×4 Gy)	6 (43)	8 (57)	0.566
10×3 Gy	15 (60)	10 (40)	
Longer-course radiotherapy (total doses >30 Gy)	16 (76)	5 (24)	

MSCC: Metastatic spinal cord compression; ECOG: Eastern Cooperative Oncology Group; bold *p*-values: significant values.

achieved with radiotherapy alone or upfront surgery is required. This information can be provided with the help of a scoring system predicting the probability to be ambulatory following radiotherapy alone. Two systems have already been developed for patients with MSCC in general, but not for specific tumor entities (4, 21). Therefore, the present study has been conducted in order to develop such a scoring system particularly for MSCC from head-and-neck cancer. Based on three predictive factors, time developing motor deficits prior to radiotherapy, pre-treatment ambulatory status and ECOG performance score, three prognostic groups were designed

with significantly different post-treatment ambulatory rates of 11% (group A), 62% (group B) and 96% (groups C), respectively. Patients of group A have a low probability of being ambulatory following radiotherapy alone and would likely benefit from the addition of upfront decompressive surgery, particularly if they meet the criteria of the randomized trial of Patchell *et al.* (6). The post-treatment ambulatory rate of group B patients is also not optimal. Thus, for these patients, upfront surgery may be considered. In group C, the post-treatment ambulatory rates at 1, 3 and 6 months following radiotherapy were extremely high with

Figure 1. Post-treatment ambulatory rates related to the scoring points.

Table III. Points for the factors included in the scoring system received by dividing post-treatment ambulatory rates (on %) by 10.

	Post-treatment ambulatory rate (%)	Points
Time developing motor deficits		
1-7 days	33	3
>7 days	77	8
Pre-treatment ambulatory status		
Not ambulatory	11	1
Ambulatory	85	9
ECOG performance score		
1-2	96	10
3-4	31	3

ECOG: Eastern Cooperative Oncology Group.

96%, 100% and 100%, respectively. Therefore, these patients appear well treated with radiotherapy alone and may not require upfront surgery. When following these suggestions, the retrospective nature of the data used to create the scoring system should be taken into consideration. Retrospective data are always associated with a risk of hidden selection biases. However, due to the fact that patients with MSCC from head-and-neck cancer are rare, prospective studies focusing on this group of patients will be very unlikely in the near future.

In this study, three predictive factors were identified regarding the ambulatory status after radiotherapy for MSCC from head-and-neck cancer. Based on these factors, a scoring system including three prognostic groups was developed. This system can help predict the probability of being ambulatory after radiotherapy alone and identify patients who could benefit from upfront decompressive surgery in this particular group of cancer patients.

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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