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Radiation Therapy for Metastatic Spinal Cord Compression in Patients with Hepatocellular Carcinoma

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Abstract. *Aim: This is the first study to investigate patients with metastatic spinal cord compression (MSCC) from hepatocellular carcinoma (HCC). Patients and Methods: Eight patients were analyzed with regard to survival and motor dysfunction. Results: Out of seven factors (age, affected vertebrae, ambulatory status, bone lesions, other distant metastases, time developing motor dysfunction, performance score) ambulatory status (p=0.005) and distant metastases (p=0.032) had a significant influence on survival. Both factors were used as a predictive tool (points: not ambulatory 0, ambulatory 1, distant metastases 0, no distant metastases 1). Total scores were 0, 1 or 2 points. Three-month survival rates were 0%, 67% and 100%, six-month survival rates 0%, 0% and 100%. Progression of motor dysfunction was prevented in 63% of patients; time developing motor deficits showed a trend (p=0.08). Conclusion: Many patients with MSCC from HCC have a short survival, which can be predicted with a new tool. Radiation therapy can stop progression of motor dysfunction.*

In recent years, a great amount of research has been carried-out to improve the treatment results in patients with hepatocellular carcinoma (HCC) which is still poor compared to several other cancer types in particular if patients present with distant metastases (1-7). If hepatocellular carcinoma patients develop bone metastases to the spine, complications such as vertebral fractures or metastatic spinal cord compression (MSCC) may occur.

Since patients with HCC account for less than 1% of those developing MSCC, very little is known on this group of patients (8). This is the first study to investigate this particular group. The present study focused on the effect of radiation therapy on motor dysfunction caused by MSCC and on the survival prognosis of these patients. Furthermore, a tool was created to predict survival of patients with MSCC from HCC and facilitate the personalization of treatment approaches. Such a tool can help the treating physicians when selecting an individualized therapy when pressed for time in an oncologic emergency situation like MSCC.

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Key Words: Hepatocellular carcinoma, metastatic spinal cord compression, radiation therapy, survival, motor dysfunction.

Patients and Methods

In the present study, the data of eight patients receiving radiation therapy alone for MSCC from hepatocellular carcinoma were analyzed regarding their effect on motor deficits and survival. In all patients, MSCC was associated with impairment of motor function in the lower extremities. Radiation therapy was delivered with photon beams from a linear accelerator to the affected vertebrae plus one additional vertebra above and below, respectively. Three different dose-fractionation regimens were used, 20 Gy in five fractions (n=2), 30 Gy in ten fractions (n=4) and 40 Gy in 20 fractions (n=2).

Seven factors were analyzed regarding the end-points mentioned in the previous paragraph, which included age (<75 *vs.* ≥75 years; median age=74.5 years), number of vertebrae affected by MSCC (1 *vs.* 2-4), ambulatory status before radiation therapy (no *vs.* yes), further bone lesions (no *vs.* yes), distant metastases in sites other than bone (no *vs.* yes), time developing motor deficits before the start of radiation therapy (1-7 *vs.* >7 days) and Eastern Cooperative Oncology Group (ECOG) performance score (2 *vs.* 3-4). Since only one patient was female, gender was not included in the analyses.

The analysis of the effect of radiation therapy was performed with the Chi-square test, and the analysis of survival with the Kaplan-Meier-method and the log-rank. Results were considered significant if a *p*-value of <0.05 was achieved. The factors that showed a significant association were additionally included in a predictive tool that is further described in the results section.

Results

According to analysis of survival (Table I), the radiation therapy regime and two other factors were significantly associated with this end-point. The two other factors were ambulatory status before radiation therapy (p=0.005) and distant metastases in sites other than bone (p=0.032). The

Table I. *Analysis of survival.*

	3 months (%)	6 months (%)	12 months (%)	*p*-Value
Age				
<75 years (n=4)	75	50	25	
≥75 years (n=4)	25	0	0	0.09
Number of affected vertebrae				
1 (n=4)	50	50	25	
2-4 (n=4)	50	0	0	0.22
Ambulatory status before RT				
No (n=3)	0	0	0	
Yes (n=5)	80	40	20	0.005
Further bone lesions				
No (n=3)	67	67	33	
Yes (n=5)	40	0	0	0.08
Distant metastases				
No (n=2)	100	100	50	
Yes (n=6)	33	0	0	0.032
Time developing motor deficits				
1-7 days (n=4)	25	0	0	
>7 days(n=4)	75	50	25	0.08
ECOG performance score				
2 (n=4)	75	50	25	
3-4 (n=4)	25	0	0	0.09
Radiation Therapy regimen				
20 Gy in 5 fractions (n=2)	0%	0%	0%	
30 Gy in 10 fractions (n=4)	50%	0%	0%	
40 Gy in 20 fractions (n=2)	100%	100%	50%	0.049

RT, Radiation Therapy; ECOG, Eastern Cooperative Oncology Group.

Table II. *Analysis the effect of radiation therapy on motor deficits.*

	Improvement (%)	No further progression (%)	Deterioration (%)	*p*-Value
Age				
<75 years (n=4)	0	75	25	
≥75 years (n=4)	0	50	50	0.56
Number of affected vertebrae				
1 (n=4)	0	75	25	
2-4 (n=4)	0	50	50	0.56
Ambulatory status before RT				
No (n=3)	0	33	67	
Yes (n=5)	0	80	20	0.30
Further bone lesions				
No (n=3)	0	67	33	
Yes (n=5)	0	60	40	0.88
Distant metastases				
No (n=2)	0	100	0	
Yes (n=6)	0	50	50	0.32
Time developing motor deficits				
1-7 days (n=4)	0	25	75	
>7 days(n=4)	0	100	0	0.08
ECOG performance score				
2 (n=4)	0	75	25	
3-4 (n=4)	0	50	50	0.56
Radiation Therapy regimen				
20 Gy in 5 fractions (n=2)	0	0	0	
30 Gy in 10 fractions (n=4)	0	75	25	
40 Gy in 20 fractions (n=2)	0	100	0	0.22

RT, Radiation Therapy; ECOG, Eastern Cooperative Oncology Group.

predictive tool developed in this study was based on both factors. The following scores were assigned: not ambulatory=0 points, ambulatory=1 point, distant metastases=0 points, no distant metastases=1 point. Therefore, total scores were either 0 (n=3), 1 (n=3) or 2 (n=2) points. The 3-month survival rates were 0% (0 points), 67% (1 point) and 100% (2 points), respectively. The six-month survival rates were 0%, 0% and 100%, respectively, and the 12-month survival rates 0%, 0% and 50%, respectively. Median survival times were 1 month, 4 months and 11 months, respectively. The p-value for the comparison of the 0-points group to the 1-point group was $p=0.022$. And the p-value for the comparison of the 1-point group to the 2-points group was $p=0.06$.

The analysis of the effect of radiation therapy on the patients' motor function revealed that improvement was observed in no patient. Further progression of motor dysfunction caused by MSCC was prevented in 63% of the patients, whereas 37% of patients showed deterioration or no improvement of complete paraplegia. The results of the analysis of the effect of radiation therapy on the patients' motor function are summarized in Table II. No factor was significantly associated with this end-point. However, the time developing motor deficits before radiation therapy was started showed a strong trend ($p=0.08$).

Discussion

Most patients with metastatic HCC have a very limited survival prognosis and need individualized treatment approaches for optimally-tailored therapies that take into account both efficacy and toxicity (1-7). If such patients present with MSCC, they are in an oncological emergency situation. Rapid treatment decisions are necessary. However, since patients with MSCC from HCC are rare, only little is known on this group, which makes a rapid decision somewhat difficult (8). Therefore, this study was initiated in order to provide data for this group and assist physicians when they have to select for the most suitable treatment regimen when under time pressure.

In this study, we were able to identify two factors that had a significant influence on the survival of patients with MSCC from HCC. These factors were the ambulatory status, before radiation therapy was started, and the presence of distant

metastases other than bone lesions. To provide a simple instrument for the physicians pressed for time, both factors were included in a predictive tool.

Such predictive tools are very important for appropriate personalization of the treatment of MSCC. Prognostic factors and predictive instruments are available for cohorts of patients with MSCC from different cancers (9-12). In addition prognostic factors have been identified (13-15) specific predictive tools have been designed (16-18) for single cancer types. The development of such specific tools is reasonable because cancer types vary considerably regarding both biological and prognostic aspects.

In the present study, the predictive survival tool consisted of three prognostic groups (0, 1 or 2 points). The median survival time of patients with 0 points was only 1 month, and no patient survived longer than 2 months. Therefore, patients with 0 points should be considered for best supportive care alone. Patients with 1 point had a median survival time of 4 months. No patient of this group survived longer than 5 months. Therefore, these patients should be considered for a radiation therapy program with an overall treatment time as short as possible. For patients with MSCC form other tumors, short-course radiation therapy was as effective as longer regimens with respect to motor function (19, 20). However, in the current study, motor dysfunction did not improve in both patients receiving 20 Gy in five fractions. Therefore, 25 Gy in five fractions may be considered for patients with 1 point. Those patients who achieved 2 points in the new survival score had a much better survival prognosis of median 11 months. Although both patients received 40 Gy in 20 fractions, radiation therapy prevented further progression but did not lead to improvement of motor dysfunction. Therefore, patients with 2 points should be considered for upfront decompressive surgery plus stabilization in addition to radiation therapy. A randomized trial demonstrated that selected patients with MSCC could benefit from additional surgery in terms of better post-treatment motor function (21).

With respect to the effect of radiation therapy on motor dysfunction, the time developing motor deficits showed a strong trend. Patients with a rapid development had a worse outcome than patients in whom the deficits developed more slowly. This result is in accordance with the findings of previous studies in patients with MSCC from different cancer types (22-24).

In conclusion, many patients with MSCC from HCC have a poor survival prognosis, although there are long-term survivors. The survival time of these patients can be predicted with a new tool. Radiation therapy can stop progression of motor deficits but likely does not improve motor function. Thus, patients with a more favorable survival prognosis should receive upfront surgical decompression and stabilization.

Conflicts of Interest

On behalf of the Authors, the corresponding Author states that there is no conflict of interest related to this study.

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