

Metastatic Spinal Cord Compression from Pancreatic Cancer

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Abstract. *Background/Aim: Pancreatic cancer is an extremely rare entity in patients with metastatic epidural spinal cord compression (MESCC). This study aimed to identify prognostic factors for functional outcome and survival following irradiation. Patients and Methods: Ten variables were investigated in 15 patients: age, gender, performance score, time from diagnosis of pancreatic cancer to MESCC, number of involved vertebrae, ambulatory status, bone metastases, organ metastases, time developing motor deficits, and the radiation schedule (1×8 Gy vs. fractionated radiotherapy schedules). Results: Better post-treatment motor function was significantly associated with absence of organ metastases (p=0.025). Better survival was also significantly associated with absence of organ metastases: 6-month survival rates were 100% and 9%, respectively (p=0.006). The radiation schedule had no significant impact on treatment outcomes. Conclusion: Patients with organ metastases have a very limited life expectancy and are good candidates for irradiation with 1×8 Gy instead of fractionated schedules.*

Metastatic epidural spinal cord compression (MESCC), which can occur in 5-10% of adult patients with cancer, is most commonly treated with radiotherapy alone (1, 2). In a palliative situation such as MESCC, personalization of the treatment is particularly important. The selection of the appropriate individual approach is facilitated if prognostic factors are known. Since each primary tumor leading to MESCC has its own biological behavior, it appears reasonable to aim to identify the specific prognostic factors of each tumor entity separately. The present study is the first

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to focus on MESCC from pancreatic cancer, a rare tumor entity in patients presenting with this oncologic emergency situation. In this study, 10 potential prognostic factors were analyzed with respect to post-treatment motor function (functional outcome) and survival.

Patients and Methods

The data of 15 patients irradiated for MESCC from pancreatic cancer were retrospectively reviewed. All patients had motor deficits of the lower extremities due to metastatic compression of the thoracic or lumbar spinal cord. Diagnosis of MESCC was confirmed with spinal computed tomography or magnetic resonance imaging. Previous surgery or radiotherapy within the involved parts of the spinal cord was not allowed. The patients were given dexamethasone from the first day of radiotherapy. Prior to radiotherapy, patients were generally presented to a surgeon. The data were collected from the patients themselves, their files, and their general practitioners or treating oncologists. The patient characteristics are summarized in Table I.

The energy used for irradiation was 6-10 MeV photons. The planning target volume included one uninvolved vertebra above and below the metastatic lesions. Motor function was assessed before radiotherapy, as well as at one month, three months and six months after radiotherapy. To categorize motor function, a 5-point scale was used: Grade 0: normal strength; grade 1: ambulatory without aid, grade 2: ambulatory with aid, grade 3: not ambulatory, grade 4: paraplegia (3). For the patient's motor function to be rated as improved or deteriorated, an alteration of at least one point on the 5-point scale must have had occurred. No patient had complete paraplegia prior to radiotherapy.

The following 10 variables were investigated for post-radiotherapy motor function and survival: age (≤60 vs. ≥61 years; median age: 61 years), gender, Eastern Cooperative Oncology Group performance score (ECOG-PS 2 vs. 3-4), time from diagnosis of pancreatic cancer to MESCC (≤12 vs. >12 months), number of involved vertebrae (1-3 vs. ≥4), pre-radiotherapy ambulatory status (not ambulatory vs. ambulatory), further bone metastases at the time of radiotherapy (no vs. yes), organ metastases at the time of radiotherapy (no vs. yes), time developing motor deficits before radiotherapy (1-7 vs. >7 days), and the radiotherapy schedule (single-fraction radiotherapy with 1×8 Gy vs. fractionated radiotherapy with 5×4 Gy in one week, 10×3 Gy in two weeks, 15×2.5 Gy in three weeks, or 20×2 Gy in four weeks).

The univariate analysis of functional outcome was performed with the ordered-logit model, because these data were ordinal (-1=deterioration, 0=no change, 1=improvement of motor function). Survival rates were calculated with the Kaplan–Meier method (4). The differences between Kaplan–Meier curves were calculated with the log-rank test. Factors that were significant ($p<0.05$) in the univariate analysis were additionally analyzed in a multivariate analysis (Cox proportional hazards model). Patients were followed up until death or for median of eight months (range=6-17 months) in those patients alive at the last follow-up visit.

Results

Of the patients included in this study, three (20%) showed an improvement, nine (60%) no further progression, and three (20%) deterioration of motor function. Table II summarizes the results of the analysis of functional outcome. An improvement of motor function was significantly associated with absence of organ metastases at the time of radiotherapy ($p=0.025$).

For the entire cohort, the 6-month survival rate was 33%. Improved survival was significantly associated with absence of organ metastases at the time of radiotherapy in both the univariate ($p=0.006$) and the multivariate ($p=0.003$) analyses. The results of the univariate analysis of survival are summarized in Table III.

Discussion

Radiotherapy alone is the most frequently administered treatment for patients presenting with MESCC. Different radiation schedules are used ranging from 1x8 Gy in one day to 20x2 Gy in four weeks. The majority of patients with MESCC have a poor survival prognosis of only a few months (1, 2). Taking into account the limited lifespan of these patients, a radiation schedule with a short overall treatment time, such as one single fraction of 8 Gy would be a good option if it is as effective as fractionated regimens. However, many radiation oncologists are quite reserved regarding the use of 1x8 Gy. This can partially be explained by the fact that fractionated longer-course radiation schedules result in better local control rates of MESCC than single-fraction radiotherapy (5,6). However, many patients with MESCC do not live long enough to experience such a recurrence. Therefore, it is important to be able to estimate the individual patient’s survival prognosis. This can be facilitated with the use of prognostic factor and scores. Since prognostic factors vary between different primary tumor types, it is important to identify the significant prognostic factors for each tumor entity. The present study was performed to compare single-fraction to multi-fraction radiation schedules and to identify significant prognostic factors for survival in patients with MESCC from pancreatic cancer. Since patients with MESCC from pancreatic cancer are extremely rare, the number of

Table I. *Patients’ characteristics.*

Characteristic	No. of patients	Proportion (%)
Age		
≤60 years	7	47
≥61 years	8	53
Gender		
Female	7	47
Male	8	53
ECOG performance score		
2	7	47
3-4	8	53
Time from cancer diagnosis to MESCC		
≤12 months	11	73
>12 months	4	27
Number of involved vertebrae		
1-3	7	47
≥4	8	53
Ambulatory status prior to radiotherapy		
Not ambulatory	5	33
Ambulatory	10	67
Further bone metastases		
No	4	27
Yes	11	73
Organ metastases		
No	4	27
Yes	11	73
Time to developing motor deficits		
1-7 days	7	47
>7 days	8	53
Radiation schedule		
1x8 Gy	3	25
Fractionated radiotherapy	12	75

ECOG: Eastern cooperative oncology group. MESCC: Metastatic epidural spinal cord compression.

patients included in this study was small. This aspect and the retrospective design of the study must be considered when interpreting our results. According to the findings of our study, a single fraction of 8 Gy was not inferior to multi-fraction schedules with respect to post-treatment motor function and may, therefore, be considered for patients with a poor survival prognosis. The presence or absence of organ metastases at the time of radiotherapy was the only prognostic factor significantly associated with survival. Thus, 1x8 Gy may be considered in particular for patients with pancreatic cancer who present with organ metastases in addition to MESCC.

The finding that 1x8 Gy is as effective as fractionated radiation schedules has previously been described in a large cohort of patients with MESCC from many different primary tumors (6). The prognostic significance of organ metastases for survival has already been identified for other tumor entities (7-9). However, for patients with MESCC from pancreatic cancer,

Table II. Impact of the potential prognostic factors on functional outcome.

Characteristic	Improvement N (%)	No change N (%)	Deterioration N (%)	<i>p</i> -Value
Age				
≤60 years	2 (29)	3 (43)	2 (29)	
≥61 years	1 (13)	6 (75)	1 (13)	0.81
Gender				
Female	1 (14)	4 (57)	2 (29)	
Male	2 (25)	5 (63)	1 (13)	0.87
ECOG performance score				
2	1 (14)	6 (86)	0 (0)	
3-4	2 (25)	3 (38)	3 (28)	0.42
Time from cancer diagnosis to MESCC				
≤12 months	2 (18)	6 (55)	3 (27)	
>12 months	1 (25)	3 (75)	0 (0)	0.76
Number of involved vertebrae				
1-3	1 (14)	4 (57)	2 (29)	
≥4	2 (25)	5 (63)	1 (13)	0.87
Ambulatory status prior to radiotherapy				
Not ambulatory	1 (20)	2 (40)	2 (40)	
Ambulatory	1 (20)	7 (70)	1 (10)	0.68
Further bone metastases				
No	1 (25)	2 (50)	1 (25)	
Yes	2 (18)	7 (64)	2 (18)	0.98
Organ metastases				
No	3 (75)	1 (25)	0 (0)	
Yes	0 (0)	8 (73)	3 (27)	0.025
Time to developing motor deficits				
1-7 days	1 (14)	4 (57)	2 (29)	
>7 days	2 (25)	5 (63)	1 (13)	0.87
Radiation schedule				
1×8 Gy	0 (0)	3 (100)	0 (0)	
Fractionated radiotherapy	3 (25)	6 (50)	3 (25)	0.68

ECOG: Eastern cooperative oncology group. MESCC: Metastatic epidural spinal cord compression.

it is the only prognostic factor significantly associated with survival. Therefore, a specific survival score for these patients is not required. Patients may be categorized with respect to their survival prognosis (poor *vs.* more favorable) simply by taking into account the presence or absence of organ metastases. This supports the idea of the variation in biological behavior of the different primary tumors leading to MESCC and the idea of aiming to identify the specific prognostic factors for each tumor entity in patients with MESCC.

In conclusion, radiotherapy of 1×8 Gy appears not to be inferior to multi-fraction radiation schedules with respect to post-treatment motor function in patients with MESCC from

Table III. Univariate analysis of survival.

Characteristic	At 6 months (%)	<i>p</i> -Value
Age		
≤60 years	29	
≥61 years	38	0.59
Gender		
Female	29	
Male	38	0.59
ECOG performance score		
2	43	
3-4	25	0.58
Time from cancer diagnosis to MESCC		
≤12 months	27	
>12 months	50	0.26
Number of involved vertebrae		
1-3	29	
≥4	38	0.59
Ambulatory status prior to radiotherapy		
Not ambulatory	20	
Ambulatory	40	0.40
Further bone metastases		
No	50	
Yes	27	0.26
Organ metastases		
No	100	
Yes	9	0.006
Time to developing motor deficits		
1-7 days	14	
>7 days	50	0.11
Radiation schedule		
1×8 Gy	0	
Fractionated radiotherapy	42	0.40

ECOG: Eastern cooperative oncology group. MESCC: Metastatic epidural spinal cord compression.

pancreatic cancer. Patients with organ metastases have a very poor survival prognosis and are good candidates for radiotherapy with 1×8 Gy instead of fractionated radiation schedules.

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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