

A Scoring Instrument to Predict the Survival Prognoses of Patients with Metastatic Epidural Spinal Cord Compression from Gynecological Malignancies

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Abstract. *Aim: To design a scoring instrument for rating overall survival (OS) of patients with metastatic epidural spinal cord compression (MESCC) from gynecological malignancies. Patients and Methods: In 22 patients treated with radiotherapy alone for MESCC from gynecological malignancies, ten factors were analyzed for effects on OS. Factors significantly associated with OS on multivariate analysis were included in a scoring instrument. Results: On multivariate analyses, no visceral metastases ($p=0.004$) and affection of 1-2 vertebrae ($p=0.012$) were significant. Scoring points for each factor were 0 or 1, depending on OS rates. After summing, scores of 0 ($n=6$), 1 ($n=9$) or 2 points ($n=9$) were obtained. OS rates were 0%, 78% and 100%, respectively, at 3 months and 0%, 33% and 86%, respectively, at 6 months ($p<0.001$). Conclusion: An instrument was developed for estimating the lifespan of patients with MESCC from gynecological malignancies. This instrument can support physicians when picking an individual treatment.*

Metastatic epidural spinal cord compression (MESCC) is an oncologic emergency that occurs in up to 10% of adult cancer patients (1, 2). Since patients with gynecological malignancies account for less than 1% of patients with MESCC, not much is known on this group. Most patients with MESCC are treated with radiotherapy alone, which was suggested to also be effective for ovarian cancer (3). Selected

patients with a good general condition and an expected lifespan of at least three months could benefit from neurosurgery prior to radiotherapy (4). Physicians should be able to rate a patient's estimated overall survival (OS) time to help them in planning treatment. Furthermore, the fractionation regimen of radiotherapy should be chosen with consideration of the patient's lifetime. It is well-agreed that patients with MESCC and a short lifespan should receive short-course radiotherapy, such as 20 Gy in 5 fractions, whereas patients with a more prolonged OS benefit from a longer-course of radiotherapy, such as 30 Gy in 10 fractions or 40 Gy in 20 fractions in terms of improved local control of MESCC and OS (2, 5, 6). Scoring instruments identifying patient groups with different OS times enable physicians to tailor treatment to a patient's individual situation. Ideally, separate instruments would be available for each tumor entity, since prognoses and biology vary considerably between primary tumors causing MESCC. This study was conducted to create a scoring instrument specifically for MESCC from gynecological malignancies.

Patients and Methods

Twenty-two patients who were treated with radiotherapy alone for MESCC from gynecological cancer were retrospectively evaluated for OS. Four patients received shorter-course radiotherapy with 1×8 in 1 day ($n=1$) or 5×4 Gy in 1 week ($n=3$), 18 patients longer-course radiotherapy with 10×3 Gy in 2 weeks ($n=9$), 15×2.5 Gy in 3 weeks ($n=3$) or 20×2 Gy in 4 weeks ($n=6$). All patients had motor weakness of the legs caused by MESCC, no prior local treatment to the involved spinal parts, surgical consultation prior to radiotherapy and diagnosis of MESCC made by computed tomography or magnetic resonance imaging. Dexamethasone was given during and tapered down following radiotherapy. Radiotherapy was delivered with 6-10 MV photon beams from a modern linear accelerator and encompassed one normal vertebra above and below those involved by MESCC.

In addition to type of radiotherapy regimen, the following nine factors were analyzed: cancer site (ovarian vs. uterine vs. cervical

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Key Words: Gynecological cancer, MESCC, radiotherapy, overall survival, scoring instrument.

vs. vulvar), age (≤ 60 vs. ≥ 61 years, median=60.5), period from diagnosis of gynecological malignancy until MESCC (≤ 15 vs. >15 months, according to previous studies), visceral metastases (no vs. yes), other bone metastases (no vs. yes), dynamic of developing weakness of the legs prior to radiotherapy (fast: ≤ 14 days vs. slow: >14 days, median=14.5 days), gait function prior to radiotherapy (not ambulatory vs. ambulatory), vertebrae affected by MESCC (1-2 vs. ≥ 3 , median=2) and Eastern Cooperative Oncology Group (ECOG) performance score (1-2 vs. 3-4). Univariate analyses were performed with the Kaplan-Meier method and the log-rank test. Factors found significant ($p < 0.05$) were additionally analyzed for independence with the Cox proportional hazards model. Factors proved to be independent predictors of OS were included in the scoring instrument.

Results

On univariate analysis, no visceral metastases ($p < 0.001$), slower (>14 days) development of weakness of the legs ($p = 0.008$), ambulatory status ($p = 0.005$), affection of only 1-2 vertebrae by MESCC ($p = 0.020$) and ECOG performance score of 0-1 ($p = 0.012$) had a significant impact on OS (Table I). Because ECOG performance score and ambulatory status were confounding variables (non-ambulatory patients had an ECOG performance score of 3-4), two multivariate analyses were performed, one including ECOG performance score and another one including ambulatory status.

On multivariate analyses, visceral metastases ($p = 0.004$) and number of vertebrae affected by MESCC ($p = 0.012$) were significant and included in the scoring instruments (Table II). The scoring points for each factor were 0 or 1 (Table III), depending on OS rates at 3 and 6 months (Table I). After summing the scoring points of both factors, prognostic scores of 0 points ($n = 6$), 1 point ($n = 9$) or 2 points ($n = 9$) were obtained. OS rates of these groups were 0%, 78% and 100%, respectively, at 3 months and 0%, 33% and 86%, respectively, at 6 months ($p < 0.001$, Figure 1).

Discussion

Personalized treatment approaches are increasingly popular for cancer patients with metastatic disease. The remaining lifespan of these palliative patients should be taken into consideration when evaluating the best available individual treatment. Therefore, several prognostic factors were identified and survival scores were developed for patients with metastatic cancer, including those with MESCC (7-10). The initial survival scores have been developed from patient cohorts with metastases from many different primary tumor types. Subsequently, the opinion has prevailed that separate scoring instruments for single tumor entities would be more appropriate to allow greater personalization of the treatment for patients with metastatic disease (2). No scoring instrument has been developed so far for patients with metastases from gynecological malignancies.

Table I. Overall survival rates at 3 and 6 months (univariate analyses).

	At 3 months (%)	At 6 months (%)	p-Value
Cancer type			
Ovarian cancer (n=8)	50	25	
Uterine cancer (n=2)	50	50	
Cervical cancer (n=11)	73	55	
Vulvar cancer (n=1)	100	0	0.26
Radiotherapy regimen			
Shorter course (n=4)	50	50	
Longer course (n=18)	67	39	0.72
Age			
< 60 years (n=11)	55	36	
≥ 61 years (n=11)	73	45	0.28
Period from cancer diagnosis until MESCC			
≤ 15 months (n=8)	38	38	
> 15 months (n=14)	79	43	0.49
Visceral metastases			
No (n=10)	100	80	
Yes (n=12)	33	8	< 0.001
Other bone metastases			
No (n=11)	91	55	
Yes (n=11)	36	27	0.06
Dynamic of developing weakness of the legs			
Fast (≤ 14 days) (n=11)	45	9	
Slow (> 14 days) (n=11)	82	73	0.008
Gait function prior to radiotherapy			
Ambulatory (n=10)	75	67	
Not ambulatory (n=12)	50	10	0.005
Number of vertebrae affected by MESCC			
1-2 vertebrae (n=13)	85	54	
≥ 3 vertebrae (n=9)	33	22	0.020
ECOG performance score			
1-2 (n=5)	100	100	
3-4 (n=17)	53	24	0.012

MESCC, Metastatic epidural spinal cord compression; ECOG, Eastern Cooperative Oncology Group; bold values, significant p -values.

In this study, a scoring instrument was developed that allows for estimation of OS in patients with gynecological cancer who experienced MESCC. Based on two independent prognostic factors, visceral metastases and the number of vertebrae affected by MESCC, an instrument was created that included three prognostic groups (0, 1 and 2 points) with significantly different OS rates. In the 0-point group, no patient survived 3 months or longer. Therefore, these patients appear to be good candidates for a less burdensome short radiotherapy program, such as 20 Gy in 5 fractions over 1 week or 8 Gy in 1 fraction, since these regimens were reported to have similar effects on motor function as longer lasting programs, such as 30 Gy in 10

Table II. Results of the multivariate analysis of overall survival.

		Hazard ratio	95%-confidence interval	p-Value
Visceral metastases	no vs. yes	14.53	2.16-154.39	0.004
Dynamic of developing weakness of the legs	≤14 vs. >14 days	1.04	0.49-2.60	0.92
Gait function prior to radiotherapy	ambulatory vs. not ambulatory	1.51	0.49-5.45	0.49
Number of vertebrae affected by MESCC	1-2 vs. ≥3 vertebrae	2.20	1.19-4.39	0.012
ECOG performance score	1-2 vs. 3-4	1.04	0.09-25.10	0.98

MESCC, Metastatic epidural spinal cord compression; ECOG, Eastern Cooperative Oncology Group; bold values, significant p-values.

fractions, 37.5 Gy in 15 fractions and 40 Gy in 20 fractions given over 2, 3 and 4 weeks, respectively (11). In the 1-point group, the majority of patients survived 3 months but only one third 6 months or longer. For these patients, radiotherapy with 20 Gy in 5 fractions appears appropriate. Highly selected patients with a good performance score may be considered for additional decompressive surgery performed prior to radiotherapy (4). Patients of the 2-point group had the most favorable OS prognosis achieving 6- and 12-month OS rates of 86% and 69%, respectively (Figure 1). These patients would likely benefit from longer lasting radiotherapy, such as 30 Gy in 10 fractions, 37.5 Gy in 15 fractions or 40 Gy in 20 fractions. These regimens were reported to achieve better local control of MESCC (freedom from an in-field recurrence of MESCC in the irradiated portion of the spine) than shorter-course programs (6, 12). The risk of developing an in-field recurrence of MSCC increases with duration of life. Thus, patients having a 2-point score carry a greater risk of a recurrence than patients of the 0-point score and the 1-point score group. Similar to the 1-point group, selected patients of the 2-point group may be considered for decompressive surgery prior to radiotherapy. When considering these recommendations, one should be aware of the small sample size of this study and the retrospective nature of the data used for creating the scoring instrument. These aspects may have led to the inclusion of hidden selection biases, which could be avoided in a prospective randomized trial. However, since patients with MESCC from gynecological cancers are scarce, trials are unlikely to be performed. Thus, retrospective data represent the best information available.

In conclusion, the new scoring instrument, including three prognostic groups with significantly different OS times, can support physicians when picking an individual treatment for patients with MESCC from gynecological malignancies.

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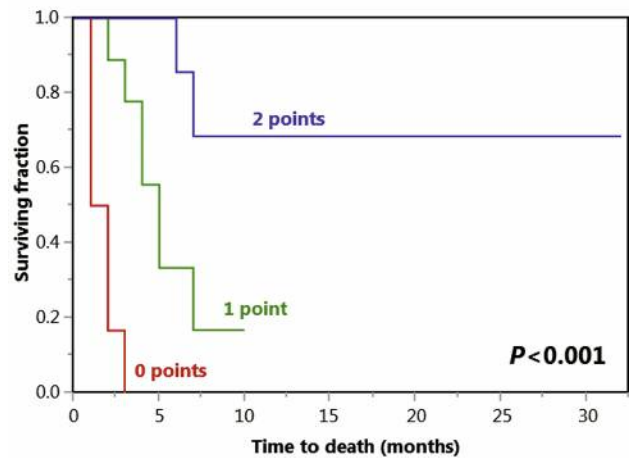


Figure 1. Kaplan-Meier curves for overall survival of patients with 0, 1 and 2 points.

Table III. Scoring points related to the factors significantly associated with overall survival on multivariate analysis.

	Scoring points
Visceral metastases	
No	1
Yes	0
Number of vertebrae affected by MESCC	
1-2 vertebrae	1
≥3 vertebrae	0

MESCC, Metastatic epidural spinal cord compression.

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Received August 16, 2016
Revised August 26, 2016
Accepted August 29, 2016