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ORIGINAL ARTICLE

A validated preoperative score predicting survival and functional outcome in lung cancer patients operated with posterior decompression and stabilization for metastatic spinal cord compression

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Abstract
Purpose This study aims to create and validate a score for survival and functional outcome of lung cancer patients with metastatic spinal cord compression (MSCC) after posterior decompressive surgery.
Methods The entire cohort of 73 consecutive patients was randomly assigned to a test group ($N = 37$) and a validation group ($N = 36$). In the test group, we retrospectively analyzed 10 preoperative characteristics. Characteristics significantly associated with survival on multivariate analysis were included in the score. Patients in the validation group were used to confirm whether the score was reproducible. Postoperative functional outcome was analyzed both in the test and validation groups.
Results On multivariate analysis, preoperative ambulatory status ($P = 0.0017$), visceral metastases ($P = 0.0002$), and time developing motor deficits ($P = 0.0004$) had significant impact on survival and were included in the scoring system. According to the prognostic scores, which ranged from 0 to 6 points, two risk groups were designed: 0–2 and 3–6 points and the median survival was 2.6 months (95 % CI, 1.0–3.8 months) and 10.7 months (95 % CI, 7.1–13.7 months), respectively ($P < 0.0001$). In the validation group, the corresponding median survival was 2.7 months (95 % CI, 1.6–5.5 months) and 10.8 months (5.8–13.6 months), respectively ($P < 0.0001$). In addition, the functional outcome was worse in patients with 0–2 points than in patients with 3–6 points both in the test ($P = 0.0023$) and validation groups ($P = 0.0298$).
Conclusion Patients with scores of 0–2 points, who have short survival time (life expectancy less than 3 months) and poor functional outcome, appear best treated with radiotherapy or best supportive care alone. Surgery may be no longer in consideration in most of the patients in this group. Patients with score of 3–6 points should be surgical candidates, because survival prognosis (life expectancy more than 10 months) and functional outcome are favorable after surgery.

Keywords Lung cancer · Metastatic spinal cord compression · Surgery · Scoring system · Prognosis

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Introduction

Approximately 28 % of the patients with lung cancer are estimated to develop metastatic spinal cord compression (MSCC) during their disease course [1]. The most appropriate treatment for MSCC is still debated. A phase III trial ($N = 101$) strongly suggested that direct decompressive surgery following postoperative radiotherapy was superior to treatment with radiotherapy alone for MSCC in 2005 [2]. Rades et al. [3] proposed the opposite result in 2010, the outcome of radiotherapy alone was not significantly inferior to those of surgery plus radiotherapy. Maranzano et al. [4] stated that the choice of radiotherapy alone or surgery in MSCC depended on accurate patient selection. Recently, only a few studies specifically addressed surgical treatment of MSCC in lung cancer [5–7]. Generally speaking, good surgical results are obtained from lung cancer patients with MSCC, while who may benefit from decompressive surgery remains unclear. Selection of the optimal treatment for the individual patient should take into account patient's estimated survival time, as well as functional outcome after therapies.

Several scoring systems have been proposed to assess survival prognosis for spinal metastasis after surgery or radiotherapy alone [8–11]. However, (1) the number of patients with lung cancer in those studies is very low, making it difficult to draw conclusions on this specific tumor type; (2) postoperative function outcome is not considered in all of those studies; (3) some old and commonly used scoring systems have underestimated the life expectancy of patients with spinal metastases of lung cancer due to the increased survival time for those patients in recent years [12, 13]. (4) Furthermore, those scores were designed for patients with spinal metastasis in general, not particularly for patients with motor impairment due to MSCC. A score for each tumor entity is really needed, since each tumor entity leading to spinal metastasis and consequent MSCC has its own biological behavior and metastatic patterns, only if specific scores are available for each of these entities can optimal treatment personalization be realized. Therefore, our present study is designed to develop and validate a survival score and analyze functional outcome particularly for patients with MSCC from lung cancer after decompressive surgery.

Methods

Study design

The entire cohort of 73 consecutive patients with lung cancer operated for MSCC were retrospectively analyzed in the study at the Affiliated Hospital of Academy of Military Medical Sciences, Beijing, between May 2005 and May 2015. All patients were operated with posterior decompression and spine stabilization. The diagnosis of bone metastasis in lung cancer patients was confirmed histologically, adequate diagnostic imaging including spinal CT or MRI, as well as bone scan. The data were collected from patients, their family members, treating surgeons, and patients' files. Approval by an ethic committee was not necessary because the data were retrospective in nature and analyzed anonymously.

The entire 73 patients were randomly divided into the test group ($N = 37$) and the validation group ($N = 36$). In the test group, we retrospectively analyzed 10 preoperative characteristics, including age (≤57 vs. ≥58 years; median age: 57 years), gender (female vs. male), histology (adenocarcinoma vs. nonadenocarcinoma), preoperative ambulatory status (ambulatory vs. not ambulatory), other bone metastases (no vs. yes), Eastern Cooperative Oncology Group Performance Status (ECOG-PS, 1–2 vs. 3–4), number of involved vertebrae (1–2 vs. ≥3), visceral metastases (no vs. yes), interval from cancer diagnosis to surgery (≤80 vs. >80 days), and the time developing motor deficits before surgery (≤14 vs. >14 days; median time: 14 days). Characteristics significantly associated with survival on multivariate analysis were included in the scoring system. The scoring point for each significant characteristic was derived from the hazard ratios on Cox proportional hazards model. The total score for each patient was obtained by adding these scoring points. Patients in the validation group were used to confirm whether the scoring system is reproducible. The characteristics related to both groups are summarized in Table 1. It demonstrates that

Table 1 Patient factors of the test group and the validation group

Factors	Test group Patients (*n*)	Validation group Patients (*n*)	*P*
Age (years)			
≤57	18	19	0.7242
≥58	19	17	
Gender			
Female	12	13	0.7405
Male	25	23	
Histology			
Adenocarcinoma	26	26	0.8539
Nonadenocarcinoma	11	10	
Preoperative ambulatory status			
Ambulatory	19	21	0.5490
Not ambulatory	18	15	
Other bone metastases			
No	7	9	0.5301
Yes	30	27	
ECOG performance status			
1–2	23	25	0.5121
3–4	14	11	
Number of involved vertebrae			
1–2	19	19	0.9029
≥3	18	17	
Visceral metastases			
No	18	19	0.7242
Yes	19	17	
Interval from cancer diagnosis to surgery (days)			
≤80	21	16	0.2928
>80	16	20	
Time developing motor deficits (days)			
≤14	18	19	0.7242
>14	19	17	

The *P* values were obtained from the Chi square test

ECOG Eastern cooperative oncology group patients in the distribution of each characteristic were similar in both the groups.

Survival analyses

The postoperative survival was defined as the time between the date of surgery and death or the latest follow-up. For the present study, we included all 73 patients with lung cancer who had decompressive surgery and stabilization due to spinal cord compression. None of the patients were excluded for any reason. 8 patients were still alive by the end of the study period, with a median follow-up of 3 months in those patients. In patients who had surgery for more than one metastasis, all sites were included in the analysis. However, only the first surgical procedure was accounted for in the survival analysis.

Surgery and functional evaluation

The indication for surgery was neurological deficit due to spinal cord compression. All patients were operated with posterior decompression and stabilization in our department. Local radiotherapy, systemic chemotherapy, and targeted therapy with gefitinib were performed after the wound healed, about 3–4 weeks after the surgery. Postoperative functional outcome was analyzed both in the test and validation groups. Neurological function was graded based on Frankel et al. [14] preoperatively and 4 weeks postoperatively (patients with Frankel D and E have the ability to walk). Time developing motor deficits was defined as the time between deterioration of motor function to disability or surgery. Deterioration of motor function was defined as a change of at least one Frankel grade.

Statistics

The univariate analysis of survival was performed using the Kaplan–Meier method and the log-rank test. The significant prognostic factors ($P < 0.05$) were additionally evaluated in a multivariate analysis performed with the Cox proportion hazards model (selection = stepwise). The prognostic factors that were significant in the multivariate analysis of the test group were included in the scoring system. The prognostic factors that were excluded by Cox proportion hazards model were not included in our scoring system. The scoring point for each significant factor was derived from the hazard ratios on Cox proportional hazards model. The total prognostic score for each patient was determined by adding the scoring points of every significant factor. Neurological outcome in risk groups was compared with Chi square test or Fisher exact test. A P value of 0.05 or less was considered statistically significant. Statistical analysis was performed using SAS 9.2 software.

Results

Basic information of the test and validation groups

The overall median survival time was 6.2 months (95 % CI, 2.9–8.8 months) in the test group and 6.0 months (95 % CI, 4.3–7.9 months) in the validation group. The corresponding 6-month survival rates were 50.3 and 47.8 % and 1-year survival rates were 23 and 20.5 %, respectively. The ten characteristics of both groups are given in Table 1. Nine patients with small cell lung cancer were also included: four patients in the test group and five patients in the validation group. Those patients did not respond well to chemotherapy and/or other conservative therapies, and half of the patients had severe neurological deficits, such as disability and incontinence.

Development of a new score

Of the investigated ten characteristics, preoperative ambulatory status ($P = 0.0054$), ECOG-PS ($P = 0.0002$), number of involved vertebrae ($P = 0.0028$), visceral metastases ($P = 0.0118$), and time developing motor deficits ($P < 0.0001$) were significantly associated with survival in the univariate analysis of the test group (Table 2). On Cox proportional hazards model, three of above five factors, preoperative ambulatory status ($P = 0.0017$), visceral metastases ($P = 0.0002$), and time developing motor deficits ($P = 0.0004$) maintained significant impact on survival and were included in the survival scoring system (Table 3). The scoring points for each of the three significant characteristics obtained from the hazard ratios on Cox proportional hazards model was seen in Table 4. The prognostic score for each patient was calculated by adding the scoring points of the three significant characteristics. The addition resulted in prognostic scores of 0, 1, 2, 3, 4, 5, and 6 points. Taking into account the 6-month survival rate of each prognostic score, the patients of the test group were divided into two risk groups: 0–2 points (group A, $n = 15$), and 3–6 points (group B, $n = 22$). The corresponding median survival times were 2.6 months (95 % CI, 1.0–3.8 months) and 10.7 months (95 % CI, 7.1–13.7 months), 6-month survival rates were 7 and 81 %, respectively ($P < 0.0001$, Fig. 1). According to the scoring system, in the validation group, the corresponding median survival times were 2.7 months (95 % CI, 1.6–5.5 months) and 10.8 months (5.8–13.6 months), and the 6-month survival rates were 14 and 77 %, respectively ($P < 0.0001$, Fig. 1).

Functional outcome

The functional outcome after surgery was worse in the group of patients with shorter survival (0–2 points) than in the group of patients with 3–6 points both in the test

Table 2 Test group: univariate analysis of preoperative factors for survival in lung cancer patients with MSCC

Factors	Patients (*n*)	Survival			*P*
		6 Mos (%)	12 Mos (%)	Median (days)	
Age (years)					
≤57	18	61	28	218	0.3802
≥58	19	39	17	136	
Gender					
Female	12	58	33	294	0.5626
Male	25	46	17	156	
Histology					
Adenocarcinoma	26	52	27	186	0.2288
Nonadenocarcinoma	11	45	11	113	
Preoperative ambulatory status					
Ambulatory	19	67	31	264	0.0054
Not ambulatory	18	33	13	100	
Other bone metastases					
No	7	57	0	213	0.8718
Yes	30	49	26	148	
ECOG performance status					
1–2	23	73	35	264	0.0002
3–4	14	14	0	90	
Number of involved vertebrae					
1–2	19	78	36	223	0.0028
≥3	18	22	7	82	
Visceral metastases					
No	18	77	36	323	0.0118
Yes	19	26	11	103	
Interval from cancer diagnosis to surgery (days)					
≤80	21	60	25	213	0.6304
>80	16	38	19	100	
Time developing motor deficits (days)					
≤14	18	28	6	82	<0.0001
>14	19	72	40	323	

MSCC metastatic spinal cord compression, *Mos* months, *ECOG* Eastern cooperative oncology group

Table 3 Test group: multivariate analysis of preoperative factors for survival in lung cancer patients with MSCC

Factors	Risk ratio	95 %-Confidence interval	*P*
Preoperative ambulatory status	4.510	1.757–11.578	0.0017
ECOG performance status		Excluded[a]	
Number of involved vertebrae		Excluded[a]	
Visceral metastases	7.913	2.678–23.382	0.0002
Time developing motor deficits	4.828	2.005–11.628	0.0004

MSCC metastatic spinal cord compression, *ECOG* Eastern cooperative oncology group

[a] Selection = stepwise, ECOG performance status and number of involved vertebrae were not included in our model

($P = 0.0023$, Table 5) and validation groups ($P = 0.0298$, Table 5). In detail, in the test group, only 27 % (4/15) of patients were able to walk (Frankel D/E) 4 weeks after surgery in group A, and 77 % (17/22) of the patients in group B; in the validation group, 63 % (10/16) of the patients were able to walk 4 weeks after surgery in group A, and 95 % (19/20) of the patients in group B.

Table 4 A new validated score for patients with lung cancer operated for MSCC

Prognostic factors	Score	No. of patients	
		Test	Validation
Preoperative ambulatory status			
Ambulatory	1	19	21
Not ambulatory	0	18	15
Visceral metastases			
No	3	18	19
Yes	0	19	17
Time developing motor deficits (days)			
≤14	0	18	19
>14	2	19	17
Prognostic groups	Total points		
Group A	0–2	15	16
Group B	3–6	22	20

MSCC metastatic spinal cord compression

In the entire cohort of 73 patients, 68.5 % (50 of 73) of the patients were able to walk 4 weeks after decompression, 8 patients died within 4 weeks after surgery and none of them achieved ambulatory status. 51.5 % (17/33) of nonambulatory patients (Frankel B/C) before operation regained the ability to walk. 82.5 % (33/40) of ambulatory patients maintained their neurological status, whereas 17.5 % (7/44) of ambulatory patients before surgery lost their ability to walk for disease progression (4 patients), postoperation complication (2 patients, wound infections), and death within 4 weeks (1 patient).

Discussion

Personalization of cancer therapy has penetrated into the sphere of oncology in recent decades. Individual strategies are particularly important for patients with MSCC, and patients with very short survival time and poor functional outcome should not be the candidates for decompressive surgery. They appear to be best treated with radiotherapy, even best supportive cares, which means less discomfort for these debilitated and enervated patients. In contrast, patient with a more favorable survival prognosis and functional outcome may benefit from decompressive surgery, which facilitates better local control of MSCC. Individual treatment approaches are often based on the patient's survival and functional prognosis which can be estimated with the help of significant prognostic factors and scoring systems.

Several prognostic factors have been identified to have statistically significant associations with survival. Better postoperative ambulatory status, improvement in neurologic status after surgery, and postoperative radiotherapy were significantly associated with longer survival which have been shown in some studies [5, 6]. However, those significant factors were in postoperative level, making it nonsense to determine whether surgical treatment is appropriate for patients before surgery.

In the present study, we analyzed 10 preoperative characteristics. Preoperative ambulatory status, ECOG-PS, number of involved vertebrae, visceral metastases, and time developing motor deficit had significant impact on survival on univariate analysis. According to the Cox proportional hazards model, three of above five significant factors, preoperative ambulatory status, visceral metastases, and time developing motor deficits, maintained significant impact on survival, which was in accordance with other studies [1, 5, 9, 10, 15]. The three preoperative factors and corresponding points are very easy to remember and obtained from patients before surgery. Ambulatory status and time developing motor deficits can be obtained from patient's sign and history, an emergency B ultrasonic can be used to determine whether liver, renal, and adrenal gland, the most common organs that lung cancer tends to metastasise to, are involved, and an X-ray can be used to make sure whether patients have primary lung cancer when patients present MSCC as the first manifestation.

Various scoring systems have been proposed for patient with spinal metastasis on the basis of retrospective data from relatively small total number of patients treated with surgery or radiotherapy alone. In 1990, Tokuhashi et al. [8] presented a score which was mostly used based on the data of 64 patients with a metastatic spine tumor who underwent spinal surgery, and only 6 patients had lung cancer. In 1995, Sioutos et al. [9] developed a score that comprised 109 patients, including 45 lung cancer patients. 10 years later, Tokuhashi has revised their score in a series of 246 patient, rarely 26 patients with lung cancer. Notably, 33.3 % (82/246) of participants were not treated with surgery in Tokuhashi's study [10]. The revised Tokuhashi score was found to be useful to predict survival for patients with spinal metastases from breast cancer alone [16] or other solid cancers [17, 18]. Unfortunately, there was no difference in neurological outcome between the three groups: the revised Tokuhashi score 0–8, 9–11 and 12–15 [17], and the data that the revised Tokuhashi score seem to be a suboptimal tool for the prediction of an individual prognosis in the group of lung cancer patients has been shown in Hessler et al. study in 2011 [12]. In their study, 67 patients with spinal metastasis from lung cancer, all of the patients underwent surgical treatment. Hessler et al. [12] concluded that the Tokuhashi scoring system underestimated the life expectancy of patients with lung cancer due to the increased survival time for this patient group. In 2013, Morgen et al. [13] also found a statistically significant increase in survival

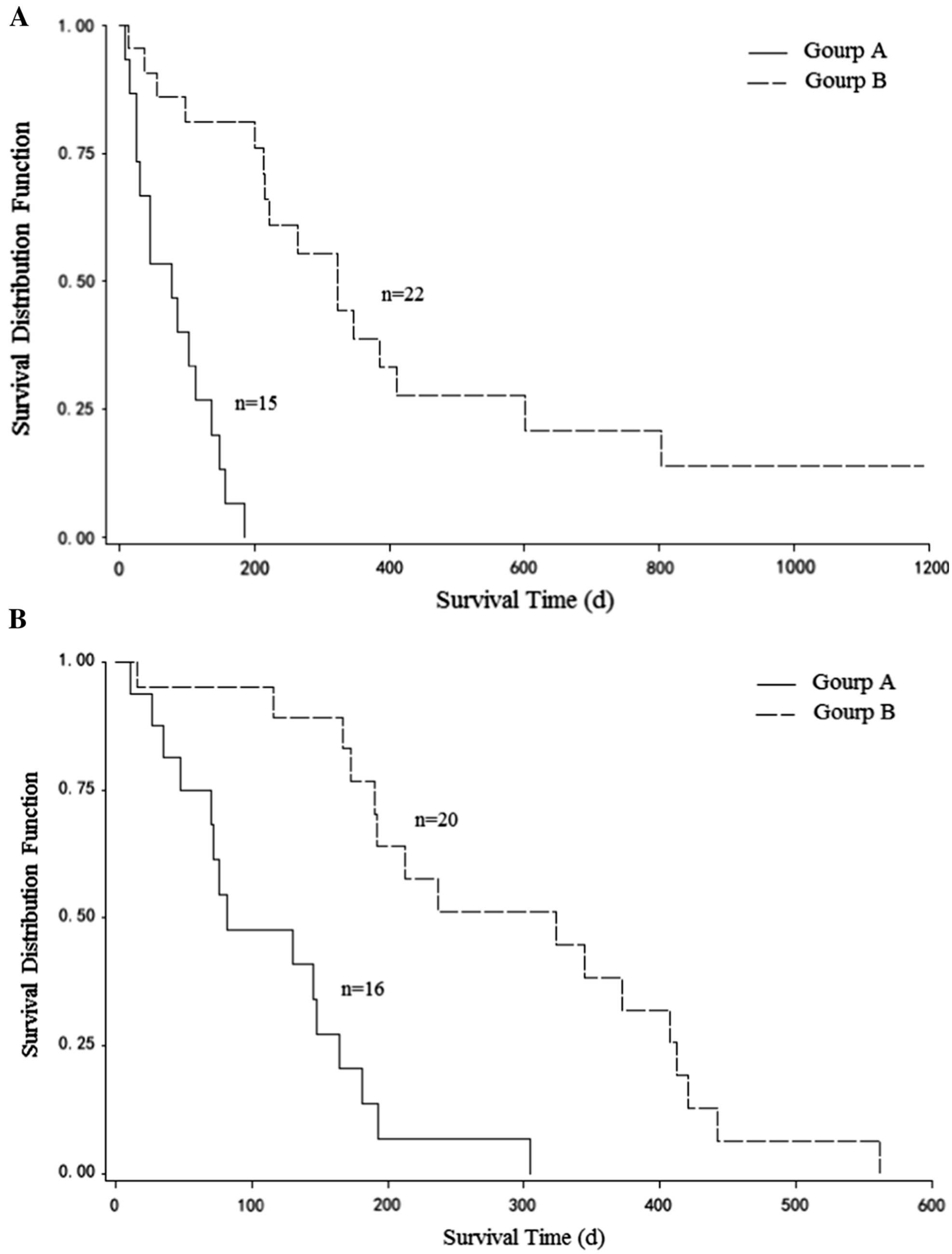

Fig. 1 Kaplan–Meier survival curves for the two risk groups of the test group (**a** $P < 0.0001$, log-rank test) and validation group (**b** $P < 0.0001$, log-rank test)

over the years for lung cancer patients with MSCC ($n = 2321$, 499 patients with lung cancer, 103 lung cancer patients were received surgical treatment). For patients with lung cancer who underwent surgery for MSCC, survival increased from 9 % in year 2005 up to 30 % in year 2010 ($P = 0.047$). In our study, overall 1-year survival is 23 % in the test group. More recent studies have reported improvements among patients with advanced lung cancer because of the new treatment options [19, 20]. With the increasing survival time of patients with lung cancer during recent years, the Tokuhashi scoring system and other scores may be no longer suitable for patents with lung cancer. Furthermore, these scores were designed for patients with spinal metastasis in general, not particularly for patients with motor impairment due to MSCC. Rades et al. [11] developed and validated a scoring system for survival of patients ($n = 356$, all patients with lung cancer) with MSCC from non-small cell lung cancer who had been treated with radiotherapy alone. Except the Rades score, the above scoring systems included relatively small number of patients with spinal metastasis from various primary tumors. In fact, participants in Rades score were received radiotherapy alone, and functional outcome was not considered in their study.

Table 5 Test and validation groups: neurological recovery of the patient in two risk groups 4 weeks after surgery, Chi square test (test group); Fisher exact test (validation group)

Groups	Risk groups	Neurological status 4 w postoperation		*P*
		Ambulatory	Not ambulatory	
Test group	A	4	11[a]	0.0023
	B	17	5[b]	
Validation group	A	10	6[c]	0.0298
	B	19	1[d]	

w weeks

[a] Four patients died within 4 weeks

[b] One patient died within 4 weeks, none of them realize ambulatory

[c] Two patients died within 4 weeks

[d] One patient died within 4 weeks, none of them realize ambulatory

In our study, a score was developed based on the data derived from 73 patients with lung cancer who underwent decompressive and stabilized surgery for MSCC. The indication for surgery is neurological deficits. Therefore, the patient's individual situation is taken more into account in the present scoring system. In order to validate our score, the risk group A and B of the test group were compared to the corresponding group A and B of the validation group. The 6-month survival rates and median survival times of the two risk groups in the validation group proved to be similar to the corresponding 6-month survival rates and median survival times of the two risk groups in the test group. Thus, this new score for MSCC from lung cancer appears valid and reproducible. Functional outcome was also considered in our study, in our scoring system, the patients group with shorter median survival (group A) also had worse neurological outcome. Functional outcome was acceptable in the entire cohort of 73 patients, 68.5 % (50 of 73) of the patients were able to walk 4 weeks after decompression; 51.5 % (17/33) of nonambulatory patients before operation regained the ability to walk. 74–84 % of patients were able to walk after surgery [2, 5] and 22–68 % of nonambulatory patients became ambulatory again in other studies [5, 7].

However, there is always patient's hope for an intervention that might preserve ambulation and drastically improve quality of life, despite poor prognosis predicted by some clinical scores. So the decision about treatment of patients with MSCC is complex and should not only rely on clinical scores. Moreover, the present scoring system is based on retrospective data, and the statistical analysis not included a relatively larger number of patients. Therefore, despite good predictive value in our scoring system, the score still warrants a prospective study to be confirmed.

In conclusion, since the survival rates and median survival of the validation group were similar to those of the test group, this score seems to be reproducible. The scoring system can help select the individual treatment for patients with metastatic spinal cord compression from lung cancer to avoid excessive and inadequate treatments. Patients with scores of 0–2 points have short survival time (Life expectancy less than 3 months) and poor functional outcome after surgery. Surgery may be no longer took into consideration in most of patient in this group, and radiotherapy alone or best supportive care can be considered. Patients with scores of 3–6 points should be surgical candidates, because survival prognosis (Life expectancy more than 10 months) and functional outcome were favorable after surgery. This scoring system appears to be valid, while a larger prospective confirmation is still needed.

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Compliance with ethical standards

Conflict of interest None.

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