Impact of Symptomatic Metastatic Spinal Cord Compression on Survival of Patients with Non-Small-Cell Lung Cancer

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OBJECTIVES: **Non-small-cell lung cancer (NSCLC) is one of the most common primary tumor sites among patients with metastatic spinal cord compression (MSCC). This disorder is related to neurologic dysfunction and can reduce the quality of life, but the association between MSCC and death is unclear. The aim of this study was to analyze the impact of the occurrence of symptomatic MSCC on overall survival of patients with NSCLC.**

METHODS: **A cohort study was carried out involving 1112 patients with NSCLC who were enrolled between 2006 and 2014 in a single cancer center. Clinical and sociodemographic data were extracted from the physical and electronic records. Survival analysis of patients with NSCLC was conducted using the Kaplan-Meier method. A log-rank test was used to assess differences between survival curves. Cox proportional hazards regression analyses were carried out to quantify the relationship between the independent variable (MSCC) and the outcome (overall survival).**

RESULTS: **During the study period, the incidence of MSCC was 4.1%. Patients who presented with MSCC were 1.43 times more likely to die than were those with no history of MSCC (hazard ratio, 1.43; 95% confidence interval [CI], 1.03–2.00; $P = 0.031$). The median survival time was 8.04 months (95% CI, 6.13–9.96) for those who presented MSCC and 11.95 months (95% CI, 10.80–13.11) for those who did not presented MSCC during the course of disease ($P = 0.002$).**

CONCLUSIONS: **MSCC is an important and independent predictor of NSCLC worse survival. This effect was not influenced by sociodemographic and clinical factors.**

INTRODUCTION

Lung cancer (LC) is the most common cancer worldwide in males and the third most common in females, accounting for almost 13% of the total cases. It is the leading cause of cancer-related death in developed countries and less economically developed countries, with an estimated 1.5 million deaths in 2012.[1] In recent years, with modern cancer therapies, the overall survival of patients with LC has improved but complications are expected to increase.[2] Non-small-cell LC (NSCLC) comprises approximately 85% of all LC cases.[3]

Many studies have found LC to be the most frequent primary tumor site among patients diagnosed with metastatic spinal cord compression (MSCC).[4-6] Morgen et al.[5] reported that LC represented 21.5% of all cases of MSCC and Phanphaisarn et al.[6] found that LC represented 41.2% of all cases of MSCC. A population-based study in patients with cancer[7] found the cumulative incidence of MSCC to be 2.5% in patients with NSCLC. MSCC is considered an oncologic emergency and without urgent treatment the spinal cord is irreversibly damaged, with permanent consequences.[8-10] Spinal involvement can cause considerable morbidity, including sensorial and motor dysfunction, severe pain, and bowel and bladder dysfunction.[9,11,12] Such neurologic complications can affect functional independence and are one of the main determinants of the quality of life in

Key words
- Cohort study
- Metastatic spinal cord compression
- Non-small-cell lung cancer
- Survival

Abbreviations and Acronyms
CI: Confidence interval
EGFR-TKI: Epidermal growth factor receptor–tyrosine kinase inhibitors
LC: Lung cancer
MSCC: Metastatic spinal cord compression
NSCLC: Non-small-cell lung cancer
PS: Performance status
RT: Radiotherapy
SD: Standard deviation

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patients with MSCC.[10,13-15] A recent systematic review[16] and a meta-analysis[17] showed that the main therapeutic modalities used alone or in combination for MSCC treatment were radiotherapy (RT), surgery, and corticosteroids and that surgery had better therapeutic efficacy regarding life expectancy and quality of life.

Numerous studies have indicated that MSCC secondary to NSCLC is associated with poorer outcomes in patients with cancer compared with the most common human cancers such as breast and prostate.[5,18,19] There is international interest in factors associated with long-term survival after diagnosis of MSCC.[19-21] On the other hand, to our knowledge, no studies have investigated the association between the occurrence of MSCC during the clinical course of NSCLC and death. It is unclear whether the occurrence of symptomatic MSCC may affect the overall survival of patients with NSCLC. Therefore, the purpose of this study was to analyze the impact of symptomatic MSCC on the overall survival of patients with NSCLC.

METHODS

A cohort study was carried out of patients diagnosed with NSCLC between 2006 and 2014, who were treated exclusively at the Brazilian National Cancer Institute (INCA). The histologic subtypes included in this study, according to the *International Classification of Diseases for Oncology, Third Edition*, were squamous cell carcinoma (codes 8050-8076), adenocarcinoma (8140-8211, 8230-8231, 8250-8260, 8323, 8480-8490, 8550-8560, 8570-8572), and large-cell carcinoma (8012-8031, 8310).

Clinical and sociodemographic data were extracted from medical records. The variables investigated were gender, age, ethnicity, marital status, years of education ($\leq$8 or >8), history of smoking (categorized as never smokers vs. smokers/former smokers), alcohol consumption (>3 times per week, independent of the amount consumed), histology, staging, body mass index, Eastern Cooperative Oncology Group performance status (PS), history of use of epidermal growth factor receptor–tyrosine kinase inhibitors (EGFR-TKI), and treatment for NSCLC. The cutoff point of 60 years was used for the age variable, according to the definition of the World Health Organization, which considers the elderly as 60 years or older in developing countries. Early-stage NSCLC was considered stage I to stage IIIa and advanced stage, stages IIIb and IV. Five treatment groups were analyzed: 1) surgery; 2) chemotherapy; 3) RT; 4) surgery combined with chemotherapy; and 5) chemotherapy combined with RT.

The MSCC was the time-dependent exposure variable of main interest, defined as indentation, displacement, or coating of the dural sac that surrounds the spinal cord or the cauda equina by an extradural tumor mass.[22] The symptomatic MSCC diagnosis was confirmed by magnetic resonance imaging or spinal computed tomography.

A descriptive analysis of the variables was compiled using median $\pm$ standard deviation (SD) for continuous variables and percentage (%) for categorical variables. A χ^2 test or Fisher exact test was used to identify differences between groups.

All patients were followed from diagnosis of NSCLC until the occurrence of symptomatic MSCC, death, date of last contact (in the case of patients lost to follow-up), or the end of the study period (i.e., April 31, 2016). A Kaplan-Meier survival analysis was conducted for the exploratory evaluation of the variables associated with the time until death. To identify whether the differences between the curves were statistically significant, the log-rank test was performed. A Cox multiple regression model using the forward stepwise method was used, aiming to estimate the independent factors associated with NSCLC death that could act as confounding or effect-modifying factors in the relationship between MSCC and death. Variables with a P value < 0.05 in the univariate analysis and clinically significant variables were selected for the multiple regression model. All statistical tests were 2 tailed. Analyses were performed with SPSS (São Paulo, Brazil) version 21.0.

This research was approved by the research ethics committee of the Brazilian National Cancer Institute (INCA) (protocol CAAE: 11556513.2.0000.5274, number 233 245/2013).

RESULTS

A total of 1112 patients diagnosed with NSCLC between 2006 and 2014 were identified and included in the analysis. **Tables 1** and **2** summarize the clinical and sociodemographic characteristics of the overall study cohort and compare patients with and without MSCC. The patients were predominantly men (61.2%), white (66.5%), living with a partner (89.1%), and with a history of smoking (88.4%). Most were PS 0–1 (74.0%), more than half of the patients (63.2%) were in the advanced stage of NSCLC, 56% were classified as eutrophic, and most of the tumors were histologically classified as adenocarcinoma (52.7%). During the study period, 45 patients (4.1%) presented with symptomatic MSCC. The median age at the time of NSCLC diagnosis was 63.0 years (range, 27–89 years $\pm$9.57 SD) in patients who did not present with MSCC and 58.0 years (range, 43–82 years $\pm$8.83 SD) in patients who presented with MSCC. Compared with patients without MSCC, patients with MSCC were more likely to be younger (55.6% vs. 40.3%; $P = 0.031$), to be nonwhite (48.9% vs. 32.9%; $P = 0.021$), to have an advanced disease stage (93% vs. 61.9%; $P < 0.001$), to have adenocarcinoma (66.7% vs. 52.1%; $P = 0.020$), to have been treated with chemotherapy or RT or chemotherapy combined with RT (93% vs. 61.9%; $P < 0.001$), and to have been treated with EGFR-TKI (11.1% vs. 3.6%; $P < 0.026$). The 2 groups (patients with and without MSCC) were similar with regard to gender, marital status, schooling, smoking, alcohol intake, body mass index, and PS.

At the time of diagnosis of MSCC, 19 patients (42.3%) presented with bowel and bladder dysfunction, 17 patients (37.8%) had no motor deficit, 13 patients (28.9%) had motor deficits but were still able to walk, 8 patients (17.8%) had severe motor deficit and could not walk, and 7 patients (15.6%) presented with paraplegia. MSCC was treated using RT in 40 patients (88.8%), surgery in 4 patients (8.8%), and 2 patients did not undergo any kind of treatment (4.4%). Thirty-four patients (75.5%) received physiotherapy during hospitalization and 20 patients (44.4%) used an orthosis for pain relief and spinal stability.

Estimates of survival time after NSCLC are presented in Table 3. The Kaplan-Meier analysis showed that better survival was associated with being female ($P < 0.001$), >8 years of study ($P = 0.012$), no history of smoking ($P = 0.007$), histologic subtype adenocarcinoma ($P < 0.001$), early stage ($P < 0.001$), PS 0–1 ($P < 0.001$), and treatment for NSCLC with surgery or surgery combined with chemotherapy ($P < 0.001$). The variables with $P < 0.05$ in the survival analysis were included in the multiple regression model.

The Cox regression analysis showed that there is an independent association between the presence of MSCC and the survival time after NSCLC. Patients who presented with MSCC were 1.43 times more likely to die than those with no history of MSCC (hazard ratio, 1.43; 95% confidence interval [CI], 1.03–2.00; $P = 0.031$), indicating that the hazardous effect of MSCC was not mediated through gender, years of education, smoking, histology, staging, PS, and treatment (Table 4).

The median survival time was 8.04 months (95% CI, 6.13–9.96) for those who presented with MSCC and 11.95 months (95% CI, 10.80–13.11) for those who did not present with MSCC during the course of disease, and this difference was statistically significant ($P = 0.002$) (Figure 1).

DISCUSSION

MSCC is the second most common neurologic complication in patients with cancer and can result in pain, paralysis, and bowel and bladder disorders.[23,24] This cohort study of patients with NSCLC diagnosed in a single cancer center between 2006 and 2014 showed that the occurrence of symptomatic MSCC during the clinical course of disease is related to worse survival, after adjusting for PS, staging, modality of treatment for NSCLC, and history of use of EGFR-TKI.

Our findings about modality of treatment and functional status are consistent with those of other studies that investigated survival in this cancer population.[25-29] A prospective cohort study of 651 patients with LC found that increased survival was associated with being selected for surgery, good PS, and early-stage disease.[25] A study by Souza et al.[26] registered 1194 patients with NSCLC and found that survival was highest in patients with good PS, initially treated with curative intent and treated with surgery for all stages. One English study using data from the National Lung Cancer Audit from 2004 to 2010 including 120,745 patients[27] showed improved survival for patients with early stage and good

Table 1. Sociodemographic Characteristics of the Population of the Study (n = 1112)

Characteristics	Total Cohort (n = 1112) n (%)	With Metastatic Spinal Cord Compression (n = 45) n (%)	Without Metastatic Spinal Cord Compression (n = 1067) n (%)	*P* Value*
Gender				0.060
Male	680 (61.2)	22 (48.9)	658 (61.7)	
Female	432 (38.8)	23 (51.1)	409 (38.3)	
Age at diagnosis (years)				**0.031**
≤60	455 (40.9)	25 (55.6)	430 (40.3)	
≥61 years	657 (59.1)	20 (44.4)	637 (59.7)	
Ethnicity				**0.021**
White	728 (66.5)	23 (51.1)	705 (67.1)	
Non-white	367 (33.5)	22 (48.9)	345 (32.9)	
Marital status				0.106
Living with partner	967 (89.1)	37 (82.2)	930 (89.4)	
Living without partner	118 (10.9)	8 (17.8)	110 (10.6)	
Years of education				0.212
≤8	556 (51.4)	20 (44.4)	536 (51.7)	
>8	526 (48.6)	25 (55.6)	501 (48.3)	
Smoking				0.438
Yes	954 (88.3)	39 (86.7)	915 (88.3)	
No	127 (11.7)	6 (13.3)	121 (11.7)	
Alcohol consumption				0.146
Yes	593 (60.6)	20 (51.3)	573 (61.0)	
No	385 (39.4)	19 (48.7)	366 (39.0)	

The statistically significant values are highlighted in bold.
*Calculated with the missing values excluded.

Table 2. Clinical Characteristics of the Population of the Study (n = 1112)

Characteristics	Total Cohort (n = 1112) n (%)	With Metastatic Spinal Cord Compression (n = 45) n (%)	Without Metastatic Spinal Cord Compression (n = 1067) n (%)	*P* Value*
Body mass index				0.897
Underweight	129 (13.7)	5 (11.9)	124 (13.8)	
Eutrophic	529 (56.3)	25 (59.5)	504 (56.1)	
Overweight/obese	282 (30.0)	12 (28.6)	270 (30.1)	
Performance status				0.519
0–1	810 (74.0)	33 (73.0)	777 (74.0)	
≥2	285 (26.0)	12 (26.7)	273 (26.0)	
Staging				**<0.001**
<IIIb	385 (36.8)	3 (7.0)	382 (38.1)	
IIIb and IV	661 (63.2)	40 (93.0)	621 (61.9)	
Histology				**0.020**
Adenocarcinoma	586 (52.7)	30 (66.7)	556 (52.1)	
Squamous cell carcinoma	496 (44.6)	12 (26.7)	484 (45.4)	
Large cell carcinoma	30 (2.7)	3 (6.7)	27 (2.5)	
Non-small-cell lung cancer treatment				**0.007**
Surgery or surgery combined with chemotherapy	237 (21.3)	3 (6.7)	234 (21.9)	
Chemotherapy or radiotherapy or chemotherapy combined with radiotherapy	875 (78.7)	42 (93.3)	833 (78.1)	
Epidermal growth factor receptor–tyrosine kinase inhibitor				**0.026**
Yes	43 (3.9)	5 (11.1)	38 (3.6)	
No	1069 (96.1)	40 (88.9)	1029 (96.4)	

The statistically significant values are highlighted in bold.
*Calculated with the missing values excluded.

PS and linked this improvement with increasing surgical resection rates. Another study[28,29] included EGFR-TKI use and showed long-term survival benefits among these patients. These results are comparable to ours, which suggests the same survival benefits. In contrast with the present study, some researchers found an association between smoking history, gender, marital status, ethnicity, and survival.[30-34] Other studies showed the importance of features that were not evaluated in this study, such as quality-of-life deficit at the time of LC diagnosis and the presence of comorbidities.[2,35]

In this sample of patients with NSCLC, we showed the association between symptomatic MSCC and death. Even after controlling for clinical covariates, MSCC still contributed significantly to the prediction of patient survival. The Cox regression analysis showed that the risk of death was 1.43 times higher among patients who presented MSCC than among those with no history of MSCC. This serious disorder already involves disability and negatively influences quality of life. To the best of our knowledge, this is the first study to show the impact of MSCC on the survival of patients with NSCLC. This disorder contributes to a longer length of hospital stay, which can result in medical complications, including pressure ulcers, venous thromboembolism, and infections. The progression of the disease, added to the myriad complications, can generate a potentiating effect for early death in patients with NSCLC and neurologic impairment caused by MSCC.

At the time of diagnosis of MSCC, more than one third of patients had no walking capacity, in the present study. The treatment for MSCC was RT in approximately 90% of cases and only 4.4% of patients underwent surgery. Nonsurgical treatment, such as RT and best supportive care, including corticosteroids and analgesics, seems to be the best treatment for patients with poor functional outcome and limited prognosis. In patients with MSCC from LC, the expected survival time is less than 3 months.[36] On the other hand, surgical decompression can benefit patients with low tumor burden and better life expectancy and functional outcome, providing local control of disease. However, the criteria for choosing the most appropriate treatment are not yet clear in these patients. In recent years, several studies[37-43] have addressed the association between the modality of treatment and the prognosis after spine metastases and MSCC from LC.

One multicenter study[42] reported the prognostic factors in a series of patients with NSCLC irradiated for MSCC between 1992 and 2010 and

Table 3. Estimates of Survival Time After Non-Small-Cell Lung Cancer

Variable	Number of Events	Time of Survival: Median	Time of Survival: (95% Confidence Interval)	Log Rank*
Gender				
Male	564	10.64	(9.65—11.63)	**<0.001**
Female	299	15.90	(13.48—18.31)	
Age to diagnostic				
≤60	349	13.37	(11.62—15.11)	0.098
61 years old or more	514	11.26	(10.00—12.53)	
Ethnicity				
White	558	11.89	(10.49—13.29)	0.086
Non-white	292	11.63	(9.96—13.29)	
Marital status				
Living with partner	754	11.56	(10.48—12.64)	0.934
Living without partner	94	13.37	(10.47—16.27)	
Years of education				
≤8	459	11.59	(10.09—13.09)	**0.012**
>8	382	12.22	(10.76—13.68)	
Smoking				
Yes	748	11.56	(10.45—12.67)	**0.007**
No	87	18.10	(13.39—22.81)	
Alcohol consumption				
Yes	478	11.59	(10.22—12.96)	0.074
No	281	12.78	(10.42—15.13)	
Histology				
Adenocarcinoma	431	14.02	(11.44—16.61)	**<0.001**
Nonadenocarcinoma	432	10.87	(9.81—11.93)	
Staging				
<IIIb	222	30.94	(23.01—38.88)	**<0.001**
IIIb and IV	584	8.67	(7.81—9.53)	
Body mass index				
Normal weight	410	11.79	(10.56—13.02)	0.054
Others	302	14.88	(12.28—17.48)	
Performance status				
0—1	584	16.49	(14.53—18.44)	**<0.001**
≥2	266	6.47	(5.59—7.35)	
Epidermal growth factor receptor—tyrosine kinase inhibitor				
Yes	35	22.47	(19.54—25.40)	0.050
No	828	11.40	(10.37—12.42)	
Non-small cell lung cancer treatment				
Chemotherapy or radiotherapy or chemotherapy combined with radiotherapy	767	9.42	(8.54—9.99)	**<0.001**
Surgery or surgery combined with chemotherapy	96	105.72	*Not available	

The statistically significant values are highlighted in bold.
*Calculated with the missing values excluded.

identified that decreased survival was associated with male gender, poor PS, non-ambulatory status before RT, involvement of more vertebrae, presence of visceral metastases, other bone metastases at the time of RT, a shorter interval from first diagnosis of NSCLC to RT of MSCC, and more rapid development of motor deficits before RT.

In the current study, patients with MSCC had reduced survival compared with those without MSCC. The median survival time was 8.04 months for those who presented with MSCC and 11.95 months for those who did not present with MSCC during the course of disease ($P = 0.002$). Recently, several scoring systems have been designed to predict survival and help to select individual therapeutic strategies for this population.[44-47] Some investigators have looked at

Table 4. Cox Regression Analysis for Risk of Death Associated with Metastatic Spinal Cord Compression in Patients with Non-Small-Cell Lung Cancer

Metastatic Spinal Cord Compression	Hazard Ratio	95% Confidence Interval	*P* Value
Univariate analysis			
Yes	1.62	1.18—2.23	0.003
No	1.00		
Adjusted analysis*			
Yes	1.43	1.03—2.00	0.031
No	1.00		

*Adjusted for staging, treatment, performance status, gender, years of education, histology, and smoking.

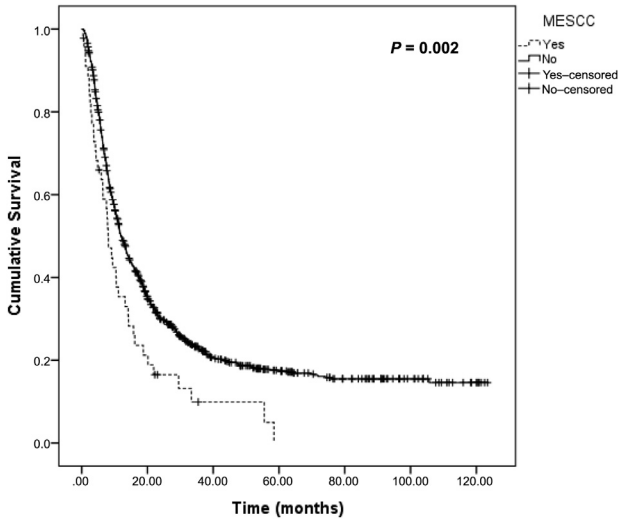

Figure 1. Time between the non-small-cell lung cancer and death. MSCC, metastatic spinal cord compression.

skeletal-related events as being prognostic factors in clinical practice and found influences on overall survival in patients with NSCLC to be similar to our results.[48-52] Skeletal-related events are considered as the presence of MSCC, pathologic fractures, malignant hypercalcemia, and requirement for RT or surgery to bone.[49,51] Bae et al.[51] reported that survival times were 8 months for patients with skeletal-related events and 15 months in patients without skeletal-related events ($P = 0.008$). Ulas et al.[50] showed that overall survival times were lower for patients who experienced skeletal-related events (7 months) than for patients with no history of skeletal-related events (12 months; $P < 0.001$). Tsuya et al.[49] presented similar results and showed that, in patients with skeletal-related events, survival was significantly shorter than that in patients without skeletal-related events (6.2 vs. 12.2 months).

This study has some limitations inherent to retrospective cohort studies that use medical records. Information about important factors could be incomplete and may have affected the data analysis. In addition, an underestimation of the number of patients with MSCC is probably a result of the difficulty of identifying subclinical cases with this condition. In addition, we used overall survival as an outcome rather than cancer-specific survival, because the cause of death derived from the registry in the hospital records may be misclassified. On the other hand, the strengths of our study include the large population size and the long period of follow-up. Regardless, future LC trials should attempt to confirm the findings of the current study and focus on whether its findings have clinical and research implications. There is evidence that the number of vertebrae involved in metastasis is associated with a higher probability of developing MSCC.[36,52] Clinicians may consider this information when recommending intensive treatment and/or surveillance for those individuals at risk and to rule out the influence of MSCC on the clinical course of NSCLC.

CONCLUSIONS

This retrospective study of a large cohort of patients found that MSCC is an important and independent predictor of abbreviated NSCLC survival. This effect was not influenced by sociodemographic and clinical factors such as staging, modality of treatment, or PS.

REFERENCES

1. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. *CA Cancer J Clin*. 2015;65:87-108.
2. Deleuran T, Thomsen RW, Nørgaard M, Jacobsen JB, Rasmussen TR, Søgaard M. Comorbidity and survival of Danish lung cancer patients from 2000-2011: a population-based cohort study. *Clin Epidemiol*. 2013;5(suppl 1):31-38.
3. Sathiakumar N, Delzell E, Morrisey MA, Falkson C, Yong M, Chia V, et al. Mortality following bone metastasis and skeletal-related events among patients 65 years and above with lung cancer: a population-based analysis of U.S. Medicare beneficiaries, 1999-2006. *Lung India*. 2013;30:20-26.
4. Mak KS, Lee LK, Mak RH, Wang S, Pile-Spellman J, Abrahm JL, et al. Incidence and treatment patterns in hospitalizations for malignant spinal cord compression in the United States, 1998-2006. *Int J Radiat Oncol Biol Phys*. 2011;80:824-831.
5. Morgen SS, Lund-Andersen C, Larsen CF, Engelholm SA, Dahl B. Prognosis in patients with symptomatic metastatic spinal cord compression. *Spine*. 2013;38:1362-1367.
6. Phanphaisarn A, Patumanond J, Settakorn J, Chaiyawat P, Klangjorhor J, Pruksakorn D. Prevalence and survival patterns of patients with bone metastasis from common cancers in Thailand. *Asian Pac J Cancer Prev*. 2016;17:4335-4340.
7. Loblaw DA, Laperriere NJ, Mackillop WJ. A population-based study of malignant spinal cord compression in Ontario. *Clin Oncol (R Coll Radiol)*. 2003;15:211-217.
8. Zairi F, Karnoub MA, Vieillard MH, Bouras A, Marinho P, Allaoui M, et al. Evaluation of the relevance of surgery in a retrospective case series of patients who underwent the surgical treatment of a symptomatic spine metastasis from lung cancer. *Eur Spine J*. 2016;25:4052-4059.
9. Cole JS, Patchell RA. Metastatic epidural spinal cord compression. *Lancet Neurol*. 2008;7:459-466.
10. Di Martino A, Caldaria A, De Vivo V, Denaro V. Metastatic epidural spinal cord compression. *Expert Rev Anticancer Ther*. 2016;12:1-10.
11. Hoskin PJ, Grover A, Bhana R. Metastatic spinal cord compression: Radiotherapy outcome and dose fractionation. *Radiother Oncol*. 2003;68:175-180.
12. Chaichana KL, Pendleton C, Sciubba DM, Wolinsky JP, Gokaslan ZL. Outcome following decompressive surgery for different histological types of metastatic tumors causing epidural spinal cord compression. *J Neurosurg Spine*. 2009;11:56-63.
13. Crnalic S, Hildingsson C, Wikström P, Bergh A, Löfvenberg R, Widmark A. Outcome after surgery for metastatic spinal cord compression in 54 patients with prostate cancer. *Acta Orthop*. 2012;83:80-86.
14. Bowers B. Recognising metastatic spinal cord compression. *Br J Community Nurs*. 2015;20:162-165.
15. Morgen SS, Engelholm SA, Larsen CF, Søgaard R, Dahl B. Health-related Quality of Life in Patients with Metastatic Spinal Cord Compression. *Orthop Surg*. 2016;8:309-315.
16. Silva GT, Bergmann A, Thuler LC. Prognostic factors in patients with metastatic spinal cord compression secondary to lung cancer: a systematic review of the literature. *Eur Spine J*. 2015;24:2107-2113.
17. Chen B, Xiao S, Tong X, Xu S, Lin X. Comparison of the therapeutic efficacy of surgery with or without adjuvant radiotherapy versus radiotherapy alone for metastatic spinal cord compression: a meta-analysis. *World Neurosurg*. 2015;83:1066-1073.
18. Tabouret E, Cauvin C, Fuentes S, Esterni B, Adetchessi T, Salem N, et al. Reassessment of

scoring systems and prognostic factors for metastatic spinal cord compression. *Spine J*. 2015;15:944-950.

19. Rades D, Weber A, Karstens JH, Schild SE, Bartscht T. Prognostic role of the number of involved extraspinal organs in patients with metastatic spinal cord compression. *Clin Neurol Neurosurg*. 2014;118:12-15.

20. Lei M, Liu Y, Liu S, Wang L, Zhou S, Zhou J. Individual strategy for lung cancer patients with metastatic spinal cord compression. *Eur J Surg Oncol*. 2016;42:728-734.

21. Tancioni F, Navarria P, Pessina F, Attuati L, Mancosu P, Alloisio M, et al. Assessment of prognostic factors in patients with metastatic epidural spinal Cord compression (MESCC) from solid tumor after surgery plus radiotherapy: a single institution experience. *Eur Spine J*. 2012;21:146-148.

22. Loblaw DA, Laperriere NJ. Emergency treatment of malignant extradural spinal cord compression: an evidence-based guideline. *J Clin Oncol*. 1998;16:1613-1624.

23. Dropcho EJ. Neurologic complications of lung cancer. *Handb Clin Neurol*. 2014;119:335-361.

24. Robson P. Metastatic spinal cord compression: a rare but important complication of cancer. *Clin Med*. 2014;14:542-545.

25. Capewell S, Sudlow MF. Performance and prognosis in patients with lung cancer. The Edinburgh Lung Cancer Group. *Thorax*. 1990;45:951-956.

26. Souza MC, Cruz OG, Vasconcelos AG. Factors associated with disease-specific survival of patients with non-small cell lung cancer. *J Bras Pneumol*. 2016;42:317-325.

27. Khakwani A, Rich AL, Powell HA, Tata LJ, Stanley RA, Baldwin DR, et al. Lung cancer survival in England: trends in non-small-cell lung cancer survival over the duration of the National Lung Cancer Audit. *Br J Cancer*. 2013;109:2058-2065.

28. Itaya T, Yamaoto N, Ando M, Ebisawa M, Nakamura Y, Murakami H, et al. Influence of histological type, smoking history and chemotherapy on survival after first-line therapy in patients with advanced non-small cell lung cancer. *Cancer Sci*. 2007;98:226-230.

29. Kaira K, Takahashi T, Murakami H, Tsuya A, Nakamura Y, Naito T, et al. Long-term survivors of more than 5 years in advanced non-small cell lung cancer. *Lung Cancer*. 2010;67:120-123.

30. Araujo LH, Baldotto CS, Zukin M, Vieira FM, Victorino AP, Rocha VR, et al. Survival and prognostic factors in patients with non-small cell lung cancer treated in private health care. *Rev Bras Epidemiol*. 2014;17:1001-1014.

31. Tammemagi CM, Neslund-Dudas C, Simoff M, Kvale P. Smoking and lung cancer survival: the role of comorbidity and treatment. *Chest*. 2004;125:27-37.

32. Wang BY, Huang JY, Cheng CY, Lin CH, Ko J, Liaw YP. Lung cancer and prognosis in Taiwan: a population-based cancer registry. *J Thorac Oncol*. 2013;8:1128-1135.

33. Tannenbaum SL, Koru-Sengul T, Zhao W, Miao F, Byrne MM. Survival disparities in non-small cell lung cancer by race, ethnicity, and socioeconomic status. *Cancer J*. 2014;20:237-245.

34. Tannenbaum SL, Zhao W, Koru-Sengul T, Miao F, Lee D, Byrne MM. Marital status and its effect on lung cancer survival. *Springerplus*. 2013;2:504.

35. Sloan JA, Zhao X, Novotny PJ, Wampfler J, Garces Y, Clark MM, et al. Relationship between deficits in overall quality of life and non-small-cell lung cancer survival. *J Clin Oncol*. 2012;30:1498-1504.

36. Silva GT, Bergmann A, Thuler LC. Incidence, associated factors, and survival in metastatic spinal cord compression secondary to lung cancer. *Spine J*. 2015;15:1263-1269.

37. Kumar N, Tan KA, Tan JH, Zaw AS, Hey HW, Ruiz J, et al. The influence of histologic subtype in predicting survival of lung cancer patients with spinal metastases [e-pub ahead of print]. *Clin Spine Surg*. 2016. https://doi.org/10.1097/BSD.0000000000000475.

38. Tang Y, Qu J, Wu J, Li S, Zhou Y, Xiao J. Metastatic spinal cord compression from non-small-cell lung cancer treated with surgery and adjuvant therapies: a retrospective analysis of outcomes and prognostic factors in 116 patients. *J Bone Joint Surg Am*. 2015;97:1418-1425.

39. Nater A, Tetreault LL, Davis AM, Sahgal AA, Kulkarni AV, Fehlings MG. Key preoperative clinical factors predicting outcome in surgically treated patients with metastatic epidural spinal cord compression: results from a survey of 438 AOSpine international members. *World Neurosurg*. 2016;93:436-448.

40. Chen YJ, Chen HT, Hsu HC. Preoperative palsy score has no significant association with survival in non-small-cell lung cancer patients with spinal metastases who undergo spinal surgery. *J Orthop Surg Res*. 2015;10:149.

41. Park SJ, Lee CS, Chung SS. Surgical results of metastatic spinal cord compression (MSCC) from non-small cell lung cancer(NSCLC): analysis of functional outcome, survival time, and complication. *Spine J*. 2016;16:322-328.

42. Rades D, Douglas S, Veninga T, Bajrovic A, Stalpers LJA, Hoskin PJ, et al. Metastatic spinal cord compression in non-small cell lung cancer patients. *Strahlentherapie und Onkologie*. 2012;6:472-477.

43. Lei M, Liu S, Yang S, Liu Y, Wang C, Gao H. New imaging characteristics for predicting postoperative neurological status in patients with metastatic epidural spinal cord compression. A retrospective analysis of 81 cases. *Spine J*. 2017;17:814-820.

44. Rades D, Conde-Moreno AJ, Segedin B, Veninga T, Cacicedo J, Schild SE. A prognostic instrument to estimate the survival of elderly patients irradiated for metastatic epidural spinal cord compression from lung cancer. *Clin Lung Cancer*. 2016;17:279-284.

45. Lei M, Liu Y, Yan L, Tang C, Yang S, Liu S. A validated preoperative score predicting survival and functional outcome in lung cancer patients operated with posterior decompression and stabilization for metastatic spinal cord compression. *Eur Spine J*. 2016;25:3971-3978.

46. Lei M, Liu Y, Tang C, Yang S, Liu S, Zhou S. Prediction of survival prognosis after surgery in patients with symptomatic metastatic spinal cord compression from non-small cell lung cancer. *BMC Cancer*. 2015;15:853.

47. Rades D, Douglas S, Veninga T, Schild SE. A validated survival score for patients with metastatic spinal cord compression from non-small cell lung cancer. *BMC Cancer*. 2012;12:302.

48. da Silva GT, Bergmann A, Thuler LC. Skeletal related events in patients with bone metastasis arising from non-small cell lung cancer. *Support Care Cancer*. 2016;24:731-736.

49. Tsuya A, Kurata T, Tamura K, Fukuoka M. Skeletal metastases in non-small cell lung cancer: A retrospective study. *Lung Cancer*. 2007;57:229-232.

50. Ulas A, Bilici A, Durnali A, Tokluoglu S, Akinci S, Silay K, et al. Risk factor for skeletal-related events (SREs) and factors affecting SRE-free survival for nonsmall cell lung cancer patients with bone metastases. *Tumour Biol*. 2016;37:1131-1140.

51. Bae HM, Lee SH, Kim TM, Kim DW, Yang SC, Wu HG, et al. Prognostic factors for non-small cell lung cancer with bone metastasis at the time diagnosis. *Lung Cancer*. 2012;77:572-577.

52. Sutcliffe P, Connock M, Shyangdan D, Court R, Kandala NB, Clarke A. A systematic review of evidence on malignant spinal metastases: natural history and technologies for identifying patients at high risk of vertebral fracture and spinal cord compression. *Health Technol Assess*. 2013;17:1-274.

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