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Original Article

Prognostic factors for overall and progression-free survival and function outcome after decompressive surgery in breast cancer patients with painful malignant spinal cord compression

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Abstract: To identify potential prognostic factors for postoperative overall and progression-free survival and analyze pain and function outcome after decompressive surgery of painful malignant spinal cord compression (MSCC) in breast cancer patients. Ten preoperative characteristics for postoperative survival in a series of thirty-nine patients with breast cancer who were operated with decompressive surgery for MSCC were retrospectively analyzed, including age, hormone receptor status at the time of diagnosis, preoperative ambulatory status, extraspinal bone metastases, Eastern Cooperative Oncology Group (ECOG) performance status, visceral metastases, preoperative chemotherapy, time developing motor deficits before surgery, pathologic compression fracture in the spine and preoperative albumin. Worst pain, average pain, and pain interference were assessed using the visual analog scale (range, 0-10) for each patient at baseline and following surgery. Function outcome was also evaluated. In the multivariate analysis, hormone receptor status at the time of diagnosis ($P = 0.04$), preoperative ambulatory status ($P = 0.01$), and visceral metastasis ($P = 0.04$) were significant associated with postoperative overall survival; hormone receptor status ($P < 0.01$), preoperative ambulatory status ($P = 0.04$), and time developing motor deficits ($P = 0.02$) were found to be significantly independent prognostic factors for progression-free survival. The average pain score in a 24-hour period was 7.2 before the operation, whereas at 1, 3, 6, and 12 months after surgery, average pain scores decreased to 3.0, 2.6, 1.9, and 2.2 (all $P < 0.001$ vs. baseline), respectively. There was significant difference between the distribution of pre- and post-operative Frankel grades ($P = 0.24$). In details, 66.7% (26/39) patients was ambulatory before operation and 87.2% (34/39) after surgery ($P = 0.03$). Surgical treatment of breast cancer patients with MSCC was found to be effective in terms of neurological recovery. Hormone receptor status at the time of diagnosis, preoperative ambulatory status, visceral metastasis, and time developing motor deficits should be considered to help physicians to select the best treatment option especially for breast cancer patients with MSCC.

Keywords: Breast cancer, spine metastasis, spinal cord compression, survival prognosis, pain outcome, function outcome

Introduction

Metastatic spinal cord compression (MSCC) occurs in approximately 10% of patients with breast cancer [1] and usually represents an oncological emergency, which involves intractable pain, neurological deficits, or even disability, negatively affecting patient's quality of remaining life [2]. The treatments of MSCC in the breast cancer patients require an integrated approach, including external radiotherapy, endocrine therapy, chemotherapy, corticosteroids, and surgery, which are often combined to give the maximum palliative effect with a minimum of morbidity and mortality, positively improving patients' quality of remaining life [3-5]. However, the most appropriate treatment for MSCC remains controversial. A prospective randomized trial showed that decompressive surgery following by radiotherapy was superior to radiotherapy alone in 2005 [6], while a matched pair analysis didn't find any benefit of

surgery followed by radiotherapy when compared with radiotherapy alone in 2010 [7]. The improvement of motor function, post-treatment ambulatory rates, and one-year overall survival rates were similar between the two groups.

Generally, life expectancy is a key factor for therapeutic planning in patients with MSCC [8]. For patients with very short survival time, radiotherapy or best supportive care alone is recommended, while for patients with more favorable prognosis, decompressive surgery or even more radical surgery is proposed to prevent the occurrence of MSCC.

Life expectancy can be estimated by prognostic factors. Unfortunately, little information is available regarding the prognostic factor and clinical outcome of breast cancer patients with MSCC after decompressive surgery. Therefore, a series of variables, including clinical characteristics (such as, age, hormone receptor status at the time of diagnosis, and preoperative ambulatory status), radiological information (such as, pathologic compression fracture in the spine) and laboratory data (such as, preoperative albumin), were retrospectively analyzed for overall survival and progression-free survival particularly in breast cancer patients with MSCC after surgery. Moreover, pain and function outcome was also analyzed in this study.

Patients and methods

Patients

The entire cohort of thirty-nine consecutive patients with breast cancer operated for MSCC were retrospectively analyzed in the study at the 307th hospital of PLA, Beijing, between March 2009 and September 2015. Inclusion criteria: (1) Patients were diagnosed with MSCC due to breast cancer. (2) Patients were treated with posterior decompression and stabilization. Exclusion criteria: (1) Primary spinal malignant tumor. (2) Intramedullary metastases. (3) Lost to follow-up. The diagnosis of breast cancer and bone metastasis was confirmed histologically, and adequate diagnostic imaging including spinal CT or MRI, as well as bone scan. Patients with asymptomatic MSCC were not included in the study. This study was approved by the Medical Research Ethics Board of the 307th hospital of PLA, which waived the need for written informed consent due to the retrospective nature of the study.

Survival analysis

Ten preoperative characteristics for postoperative overall and progression-free survival were retrospectively analyzed: age (≤ 5 years vs. > 51 years; median age: 51 years), hormone receptor status at the time of diagnosis (positive vs. negative), preoperative ambulatory status (ambulatory vs. not ambulatory), extraspinal bone metastases (no vs. yes), Eastern Cooperative Oncology Group (ECOG) performance status (1-2 vs. 3-4), pathologic compression fracture in the spine (no vs. yes), visceral metastases (no vs. yes), preoperative chemotherapy (no vs. yes), time developing motor deficits before surgery (≤ 14 days vs. > 14 days, median time: 14 days), and preoperative albumin (≤ 35 g/l vs. > 35 g/l, conformed to previous studies).

Postoperative survival was the length of time from surgery to death or to the last follow-up date, and patients who were alive at the last follow-up were censored in the postoperative survival analysis. Progression-free survival was defined as the time interval between surgery and progression, death, or the last follow-up date, whichever occurred first. Patients who were alive without progression were censored in the progression-free survival analysis. Progression was defined as tumor size enlargement on MRI, increase in the extent of hypermetabolism on positron emission tomography-computed tomography, or new lesion development during follow-up. 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. Ambulatory means that a patient can take at least two steps with each foot with or without a cane or walker. We collected data from outpatient systems and telephone interviews. The last follow-up date was in December, 2016.

Pain and function analysis

The indication for surgery was neurological deficits due to spinal cord compression which had been confirmed by spinal magnetic resonance imaging. Patients also had to have a general

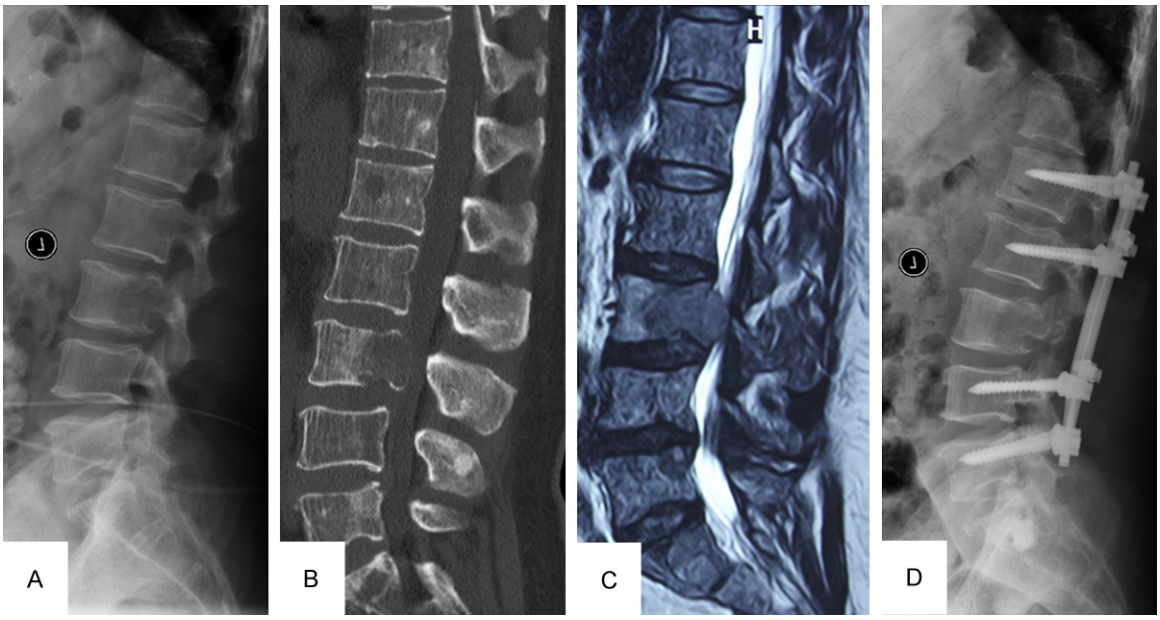

Figure 1. A 52-year-old female who was unable to walk due to metastatic spinal cord compression (MSCC) resulted from breast cancer. (A) Preoperative X-ray showed bone destruction and pathologic collapse of L3. (B) Preoperative CT showed bone destruction and pathologic collapse of L3. (C) Preoperative MRI showed MSCC at L3. (D) Following laminectomy at L2-L3, and pedicle screw fixation was conducted to spine stabilization. Postoperative motor function was improved from Frankel (C) to (D). She died at postoperative 7.2 months and spine stability was maintained throughout the survival period.

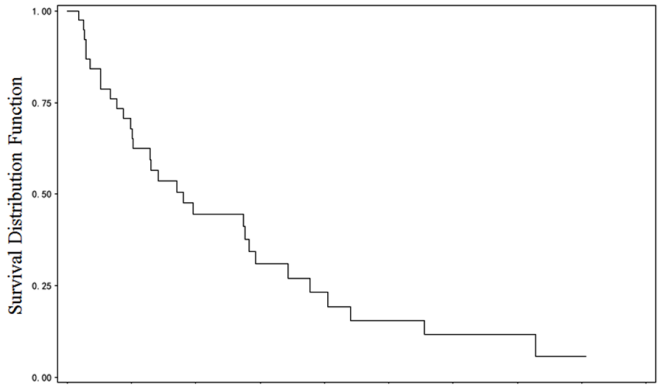

Figure 2. Kaplan-Meier survival curves for postoperative overall survival.

medical status good enough to be acceptable surgical candidates and an expected survival of at least 3 months which was estimated by Lei scoring system [9]. All patients were operated with decompressive surgery and spine stabilization (**Figure 1**). Local radiotherapy, systemic chemotherapy, bisphosphonate therapy and targeted therapy then were performed after the wound healed, about 3-4 weeks after the surgery. Patients with positive hormone receptor were recommended with endocrine therapy. Worst pain, average pain, and pain interference were assessed using the visual analog scale (range, 0-10) for each patient at baseline and following surgery. Neurological function was graded based on Frankel et al. [10] preoperatively and 4 weeks postoperatively (patients with Frankel D and E were ambulatory).

Statistical methods

The Kaplan-Meier method was used to evaluate postoperative and progression-free survival. The univariate and multivariate analysis of postoperative and progression-free survival were estimated by the simple and multiple Cox proportional hazards regression models, respectively. *Kappa* test, Wilcoxon rank test or Kruskal-Wallis rank test, and Chi-square test were performed to analyze function outcome after surgery. Repeated measures the correlated variance model across each time points, supplemented by Wilcoxon rank-sum test, was performed to analyze pain outcome. A *P* value of

Table 1. Univariate and multivariate analysis of preoperative factors for postoperative survival in breast cancer patients with MSCC

Factors	Patients (n)	Simple Cox regression		Multiple Cox regression	
		HR (95% CI)	*P*	HR (95% CI)	*P*
Age					
≤ 51 years	21				
> 51 years	18	0.99 (0.48-2.03)	0.97	Not included	
Hormone receptor status at the time of diagnosis					
Positive	25				
Negative	14	2.47 (1.19-5.15)	0.01	2.11 (1.01-4.42)	0.04
Preoperative ambulatory status					
Ambulatory	26				
Not Ambulatory	13	2.71 (1.26-5.83)	0.01	2.71 (1.24-5.95)	0.01
Extraspinal bone metastases					
No	11				
Yes	28	1.58 (0.69-3.64)	0.27	Not included	
ECOG Performance status					
1-2	22				
3-4	17	1.86 (0.87-4.01)	0.11	Not included	
Pathologic compression fracture in the spine					
No	17				
Yes	22	0.93 (0.45-1.93)	0.85	Not included	
Visceral metastases					
No	19				
Yes	20	2.21 (1.04-4.70)	0.03	2.21 (1.03-4.75)	0.04
Preoperative chemotherapy					
No	7				
Yes	32	2.37 (0.99-5.65)	0.05	Not included	
Time developing motor deficits					
≤ 14 days	19				
> 14 days	20	2.49 (1.17-5.32)	0.01	Not included	
Preoperative albumin					
≤ 35 g/l	16				
> 35 g/l	23	1.31 (0.63-2.74)	0.46	Not included	

Abbreviations: MSCC, Metastatic spinal cord compression; ECOG, Eastern Cooperative Oncology Group; HR, hazard ratio; CI, confidence interval.

0.05 or less was considered statistically significant. Statistical analysis was performed using SAS 9.2 software.

Results

Patient characteristics

Of the total series of thirty-nine patients, thirty-six patients (92.3%) were treated with radical resection of primary breast cancer and seven patients (17.9%) were diagnosed with bone metastasis at initial breast cancer diagnosis. All patients were female, and the median age was 51 years old (range, 34-70 years old). The median postoperative overall survival was 15.0 months (95% CI, 8.4-24.4 months), 1-year and 5-year postoperative overall survival rates were 53.5% and 5.8%, respectively (**Figure 2**). The median progression-free survival was 10.3 months (95% CI, 6.1-14.9 months), 1-year and 5-year progression-free survival rates were 43.4% and 0.0%, respectively. At the latest follow up, seven patients (17.9%, 7/39) were alive with a mean follow-up of 23.9 months (range, 2.1-67.2 months), and four patients (10.3%,

Table 2. Univariate and multivariate analysis of preoperative factors for progression-free survival in breast cancer patients with MSCC

Factors	Patients (n)	Simple Cox regression		Multiple Cox regression	
		HR (95% CI)	*P*	HR (95% CI)	*P*
Age					
≤ 51 years	21				
> 51 years	18	0.78 (0.39-1.54)	0.47	Not included	
Hormone receptor status at the time of diagnosis					
Positive	25				
Negative	14	3.17 (1.53-6.55)	0.01	2.85 (1.36-5.96)	0.01
Preoperative ambulatory status					
Ambulatory	26				
Not Ambulatory	13	2.72 (1.30-5.67)	0.01	2.11 (1.01-4.40)	0.04
Extraspinal bone metastases					
No	11				
Yes	28	1.50 (0.69-3.25)	0.31	Not included	
ECOG performance status					
1-2	22				
3-4	17	1.97 (0.96-4.03)	0.06	Not included	
Pathologic compression fracture in the spine					
No	17				
Yes	22	1.22 (0.61-2.45)	0.58	Not included	
Visceral metastases					
No	19				
Yes	20	1.76 (0.88-3.51)	0.11	Not included	
Preoperative chemotherapy					
No	7				
Yes	32	1.95 (0.83-4.58)	0.12	Not included	
Time developing motor deficits					
≤ 14 days	19				
> 14 days	20	2.72 (1.26-5.88)	0.01	2.50 (1.16-5.40)	0.02
Preoperative albumin					
≤ 35 g/l	16				
> 35 g/l	23	1.39 (0.70-2.78)	0.35	Not included	

Abbreviations: MSCC, Metastatic spinal cord compression; ECOG, Eastern Cooperative Oncology Group; HR, hazard ratio; CI, confidence interval.

4/39) were alive without disease progression with a mean follow-up of 15.9 months (range, 2.1-48.6 months).

Prognostic factors

In the univariate analysis, postoperative survival was associated with hormone receptor status at the time of diagnosis (HR = 2.47; 95% CI, 1.19-5.15; *P* = 0.01), preoperative ambulatory status (HR = 2.71; 95% CI, 1.26-5.83; *P* < 0.01), visceral metastasis (HR = 2.21; 95% CI, 1.04-4.70; *P* = 0.03), and time developing motor deficits (HR = 2.49, 95% CI, 1.17-5.32; *P* = 0.01, **Table 1**). Preoperative chemotherapy led to a longer postoperative survival, but it showed no significance. In the multivariate analysis of postoperative survival, hormone receptor status at the time of diagnosis (HR = 2.11; 95% CI, 1.01-4.42; *P* = 0.04), preoperative ambulatory status (HR = 2.71; 95% CI, 1.24-5.95; *P* = 0.01), and visceral metastasis (HR = 2.21; 95% CI, 1.03-4.75; *P* = 0.04) were significant, whereas other variables were not included in the multiple Cox proportional hazards regression model.

Regarding progression-free survival, hormone receptor status at the time of diagnosis (HR = 3.17; 95% CI, 1.53-6.55; *P* < 0.01), preopera-

Table 3. Brief inventory of VAS at baseline and following surgery

Pain	Baseline N = 39	1 months N = 39	3 months N = 31	6 months N = 28	12 months N = 18
Worst pain (0-10)					
Score	8.2	4.9	4.0	3.4	3.6
P		0.001	0.001	0.001	0.001
Average pain (0-10)					
Score	7.2	3.0	2.6	1.9	2.2
P		0.001	0.001	0.001	0.001
Pain interference (0-10)					
Score	7.6	3.4	3.1	2.0	2.2
P		0.001	0.001	0.001	0.001

VAS indicates visual analog scale.

tive ambulatory status (HR = 2.72; 95% CI, 1.30-5.67; $P < 0.01$), and time developing motor deficits (HR = 2.72, 95% CI, 1.26-5.88; $P = 0.01$) had significant impact according to the univariate analysis (**Table 2**). Favorable ECOG performance status showed a longer progression-free survival, but it had no significance. According to the multivariate analysis, hormone receptor status at the time of diagnosis (HR = 2.85; 95% CI, 1.36-5.96; $P < 0.01$), preoperative ambulatory status (HR = 2.11; 95% CI, 1.01-4.40; $P = 0.04$), and time developing motor deficits (HR = 2.50, 95% CI, 1.16-5.40; $P = 0.02$) were found to be significantly independent prognostic factors.

VAS outcome

The mean worst pain score in a 24-hour period was 8.2 before the operation, whereas at 1, 3, 6, and 12 months after surgery, mean worst pain scores decreased to 4.9, 4.0, 3.4, and 3.6 (all P < 0.001 vs. baseline, **Table 3**), respectively. The average pain score in a 24-hour period was 7.2 before the operation, whereas at 1, 3, 6, and 12 months after surgery, average pain scores decreased to 3.0, 2.6, 1.9, and 2.2 (all P < 0.001 vs. baseline), respectively. The mean pain interference score in a 24-hour period was 7.6 before the operation, whereas at 1, 3, 6, and 12 months after surgery, mean pain interference scores decreased to 3.4, 3.1, 2.0, and 2.2 (all P < 0.001 vs. baseline), re spectively. In detail, the worst pain relief (a 2-score drop in pain was defined as clinically significant relief) was observed in 82.1% of the patients, the average pain relief was achieved in 89.7% of the patients, and pain interference relief occurred in 84.6% of the patients after surgery.

Function outcome

The distribution of pre- and post-operative Frankel grades was shown in **Table 4**. There was no significant consistency between the distributions of Frankel grades before surgery and those after surgery ($P = 0.19$), which suggested that decompressive surgery changed the function outcome. The distribution of the total of Frankel grades after surgery was significant difference when compared with those before surgery ($P < 0.01$). In details, 66.7% (26/39) patients was ambulatory before surgery and 87.2% (34/39) patients became ambulatory after surgery ($P = 0.03$). In the entire cohort of 39 patients, all ambulatory patients maintained their neurological status, and 61.5% (8/13) nonambulatory patients before operation regained the ability to walk after surgery.

Discussion

Since life expectancy is of such great influence on therapeutic decision-making in patients with MSCC, its accurate prediction, which can be estimated with the help of significant prognostic factors, is of the utmost importance. Previously, we found that postoperative survival was significantly associated with type of primary tumor, preoperative ambulatory status, visceral metastasis, and targeted therapy in a series of 95 patients [11]. However, those significant factors were identified in patients with MSCC resulted from various primary cancer, making it nonsense to help surgeons to select appropriate techniques particularly for breast cancer patients with MSCC.

Fortunately, several studies have reported some factors affecting survival prognosis in patients with MSCC especially resulted from breast cancer. Rades et al. [12, 13] found that survival was negatively affected by the presence of visceral metastases, deterioration of motor function after radiation, reduced performance status, and the rapid development of

Table 4. Neurological recovery of the breast cancer patient with MSCC before and 4 weeks after operation

Neurological status before operation		Neurological status 4 weeks after operation					Total[a]	Total[b]
		Not ambulatory			Ambulatory			
		A	B	C	D	E		
Not ambulatory	A	0	0	1	1	0	2	13
	B	0	1	1	2	0	4	
	C	0	1	1	3	2	7	
Ambulatory	D	0	0	0	13	13	26	26
	E	0	0	0	0	0	0	
Total[a]		0	2	3	19	15	39	$P_1 = 0.19$
Total[b]		5			34		$P_2 = 0.01$	$P_3 = 0.03$

[a]Regarding Frankel grades; [b]Regarding ambulatory status (Frankel D/E has the ability to walk). P_1 The distribution of Frankel grades before operation compared with those after operation, Kappa test; P_2 The total of Frankel grades before operation compared with those after operation, Wilcoxon rank test or Kruskal-Wallis rank test. P_3 The difference of ambulatory status between pre- and post-operation, Chi-square test. Abbreviations: MSCC, Metastatic spinal cord compression.

motor deficits. Reinert et al. [14] reported the essential prognostic factors that correlated with survival were Tokuhashi score, performance status, presence of visceral metastasis, and interval between symptoms and radiotherapy. Bergmann et al. [1] showed that the only variable that was associated with increased survival after compression syndrome was the use of bisphosphonates after bone metastasis. However, participants in the above-mentioned studies received radiation instead of surgery. Further, radiological information, laboratory data, and systematic treatment were not considered in their studies. Notably, some studies have showed that those factors might be associated with survival prognosis in patients with MSCC [15, 16]. Finally, function outcome was not analyzed in all above studies. To our knowledge, function status plays an important role in the patient's quality of remaining life for patients with advanced cancer.

In the present study, hormone receptor status at the time of diagnosis, preoperative ambulatory status, and visceral metastasis had significant impact on postoperative survival, which was in accordance with other studies [17-19]. Moreover, we also found that hormone receptor status at the time of diagnosis, preoperative ambulatory status, and time developing motor deficits were significantly independent prognostic factors for progression-free survival. In the entire cohort of thirty-nine patients, the median survival time was 15 months, and 3-34 months was shown in other studies [1, 14, 15, 20, 21]. The median progression-free survival was 10.3 months. Cho et al. [22] found that the mean progression-free survival was 11.82 months in a series of 46 cervical spine metastasis, and he also showed that postoperative adjuvant therapy was significantly associated with progression-free survival. The pain outcome assessed by worst pain score, average pain score, and pain interference score was remarkably decreased after surgery. Regarding function outcome, there was no significant consistency between the distributions of Frankel grades before surgery and those after surgery, which suggested that decompressive surgery changed the function outcome. Function outcome was more favorable after surgery when compared with those before surgery. In details, 66.7% (26/39) patients were ambulatory before surgery and 87.2% (34/39) patients were ambulatory after surgery (P = 0.03). Previous studies reported that 68% to 84% patients with spine metastasis were ambulatory after decompressive surgery [6, 23]. Importantly, pre-treatment ambulatory status has a significant influence on post-treatment ambulatory status [24], which was consistent with the present study.

However, our study had some limitations. On the one hand, this was a retrospective evaluation of data collected from patient's files, so a hidden selection bias cannot be excluded. On the other hand, the statistical analysis didn't include a relatively larger number of patients. Therefore, a prospective study is still warranted.

In summary, surgical treatment of breast cancer patients with MSCC was found to be effective in terms of neurological recovery and local tumor control. Besides, hormone receptor status at the time of diagnosis, preoperative ambulatory status, visceral metastasis, and time developing motor deficits should be considered to help physicians to select the best treatment option especially for patients with MSCC resulted from breast cancer. For patients with positive hormone receptor, ambulatory, no visceral metastasis, and slowly developing motor deficits, surgery should be considered. However, great care should be taken in cases with negative hormone receptor, non-ambulatory, visceral metastasis, and rapidly developing motor deficit. Importantly, hormone receptor status at the time of diagnosis and preoperative ambulatory status should always be carefully evaluated, because those factors were found to be related to both overall and progression-free survival. Still, a lager prospective study is needed.

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Disclosure of conflict of interest

None.

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References

[1] Bergmann A, Fabro EN, Silva BA. Survival of women with spinal compression syndrome due to bone metastasis secondary to breast cancer. Rev Neuro 2014; 22: 195-200.

[2] Robson P. Metastatic spinal cord compression: a rare but important complication of cancer. J R Coll Physicians Lond 2014; 14: 542-5.

[3] Shiue K, Sahgal A, Chow E, Lutz ST, Chang EL, Mayr NA, Wang JZ, Cavaliere R, Mendel E, Lo SS. Management of metastatic spinal cord compression. Expert Rev Anticancer Ther 2010; 10: 697-708.

[4] Joaquim AF, Powers A, Laufer I, Bilsky MH. An update in the management of spinal metastases. Arq Neuropsiquiatr 2015; 73: 795-802.

[5] Laufer I, Rubin DG, Lis E, Cox BW, Stubblefield MD, Yamada Y, Bilsky MH. The NOMS framework: approach to the treatment of spinal metastatic tumors. Oncologist 2013; 18: 744-51.

[6] Patchell RA, Tibbs PA, Regine WF, Payne R, Saris S, Kryscio RJ, Mohiuddin M, Young B. Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial. Lancet 2005; 366: 643-8.

[7] Rades D, Huttenlocher S, Dunst J, Bajrovic A, Karstens JH, Rudat V, Schild SE. Matched pair analysis comparing surgery followed by radiotherapy and radiotherapy alone for metastatic spinal cord compression. J Clin Oncol 2010; 28: 3597-604.

[8] 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: 185.

[9] Lei M, Li J, Liu Y, Jiang W, Liu S, Zhou S. Who are the best candidates for decompressive surgery and spine stabilization in patients with metastatic spinal cord compression?: a new scoring system. Spine 2016; 41: 1469-76.

[10] Frankel HL, Hancock DO, Hyslop G, Melzak J, Michaelis LS, Ungar GH, Vernon JD, Walsh JJ. The value of postural reduction in the initial management of closed injuries of the spine with paraplegia and tetraplegia. Paraplegia 1969; 7: 179-92.

[11] Lei M, Liu Y, Yan L, Tang C, Liu S, Zhou S. Posterior decompression and spine stabilization for metastatic spinal cord compression in the cervical spine. A matched pair analysis. Eur J Surg Oncol 2015; 41: 1691-8.

[12] Rades D, Veninga T, Stalpers LJ, Schulte R, Hoskin PJ, Poortmans P, Schild SE, Rudat V. Prognostic factors predicting functional outcomes, recurrence-free survival, and overall survival after radiotherapy for metastatic spinal cord compression in breast cancer patients. Int J Radiat Oncol Biol Phys 2006; 64: 182-8.

[13] Rades D, Conde AJ, Garcia R, Cacicedo J, Segedin B, Perpar A, Schild SE. A new instrument for estimation of survival in elderly patients irradiated for metastatic spinal cord compression from breast cancer. Radiat Oncol 2015; 10: 173.

[14] Reinert T, Zylberberg R, Lima FMT, et al. Prognostic factors predicting overal survival after radiotherapy for metastatic spinal cord

compression in breast cancer patients treated in the Brazilian public health system. Cancer Res 2015; 75: Suppl 1.
[15] Guo Y, Young B, Palmer JL, Mun Y, Bruera E. Prognostic factors for survival in metastatic spinal cord compression: a retrospective study in a rehabilitation setting. Am J Phys Med Rehabil 2003; 82: 665-8.
[16] Switlyk MD, Kongsgaard U, Skjeldal S, Hald JK, Hole KH, Knutstad K, Zaikova O. Prognostic factors in patients with symptomatic spinal metastases and normal neurological function. Clin Oncol 2015; 27: 213-21.
[17] Ahn SG, Lee HM, Cho SH, Lee SA, Hwang SH, Jeong J, Lee HD. Prognostic factors for patients with bone-only metastasis in breast cancer. Yonsei Med J 2003; 54: 1168-77.
[18] Rades D, Douglas S, Schild SE. A validated survival score for breast cancer patients with metastatic spinal cord compression. Strahlenther Onkol 2013; 189: 41-6.
[19] Bollen L, Wibmer C, Wang M, van der Linden YM, Leithner A, Bünger CE, Jensen AB, Fiocco M, Bratschitsch G, Pondaag W, Bovée JV, Dijkstra PD. Molecular phenotype is associated with survival in breast cancer patients with spinal bone metastases. Clin Exp Metastasis 2015; 32: 1-5.
[20] Bollen L, de Ruiter GC, Pondaag W, Arts MP, Fiocco M, Hazen TJ, Peul WC, Dijkstra PD. Risk factors for survival of 106 surgically treated patients with symptomatic spinal epidural metastases. Eur Spine J 2013; 22: 1408-16.
[21] Walcott BP, Cvetanovich GL, Barnard ZR, Nahed BV, Kahle KT, Curry WT. Surgical treatment and outcomes of metastatic breast cancer to the spine. J Clin Neurosci 2011; 18: 1336-9.
[22] Cho W, Chang UK. Neurological and survival outcomes after surgical management of subaxial cervical spine metastases. Spine 2012; 37: E969-77.
[23] 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.
[24] Turner S, Marosszeky B, Timms I, Boyages J. Malignant spinal cord compression: a prospective evaluation. Int J Radiat Oncol 1993; 26: 141-6.