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Original Article

Prognostic factors and surgical outcome after decompressive surgery in aged patients with metastatic spinal cord compression

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Abstract: To identify potential prognostic factors predicting postoperative survival and function outcome and to analyze surgical outcome after decompressive surgery of metastatic spinal cord compression (MSCC), especially in aged patients. Eleven preoperative characteristics for postoperative survival and functional outcome in a series of fifty-four aged patients with MSCC who were operated on with decompressive surgery were retrospectively analyzed. These characteristics included gender, primary site, preoperative ambulatory status, ECOG performance status, number of involved vertebrae, visceral metastases, preoperative chemotherapy, bone metastasis at cancer diagnosis, the time developing motor deficits, preoperative albumin, and radical surgery at primary site. In multivariate analysis, primary site (HR, 2.33, 95% CI: 1.50-3.62; P<0.01) and visceral metastases (HR, 4.58, 95% CI: 2.21-9.48; P<0.01) were significantly associated with postoperative survival. Preoperative ambulatory status (HR, 4.98, 95% CI: 1.10-22.55; P=0.04) and visceral metastases (HR, 6.41, 95% CI: 1.43-28.77; P=0.02) were found to be significantly independent prognostic factors for postoperative function outcome. There was no significant consistency between the distribution of pre-operative and post-operative Frankel grades (P=0.20). The distribution of the total of Frankel grades after surgery was significantly different as compared with those before surgery (P=0.01). Eighteen complications were recorded within four weeks of surgery in 27.8% (15/54) of patients. Surgical treatment of aged patients with MSCC was found to be effective in terms of neurological recovery with a tolerable rate of complications. Primary site, visceral metastases, and preoperative ambulatory status should be considered to help physicians select the best treatment option, especially for aged patients with MSCC.

Keywords: Aged patients, spine metastasis, spinal cord compression, surgery, prognosis

Introduction

Thanks to the development of molecularly targeted interventions, chemotherapies, and systematic treatments cancer patients are living longer and growing older [1-3]. Aged patients usually have a poor tolerance to treatment, worse immune systems, and a relatively shorter life expectancy. These present challenges are for surgeons, in making a surgical decision, especially in those with metastatic spinal cord compression (MSCC). MSCC often occurs as an oncological emergency in approximately 5%-14% of patients with advanced cancer. MSCC involves intractable pain, weakness, incontinence, and even disability negatively affecting the aged patient's quality of remaining life [4, 5]. Notably, with careful patient selection, surgery can achieve long duration of ambulation in aged patients with MSCC [6]. Thus, in order to remarkably maximize the quality of life, personalized approaches are needed to avoid excessive and inadequate treatments. Such personalization should take into account an individual patient's survival time and function outcome after treatments, which can be estimated with the help of predictive prognostic factors.

Therefore, we retrospectively analyzed eleven preoperative characteristics for postoperative survival and function outcome particularly in aged patients with MSCC after decompressive surgery.

Patients and methods

Fifty-four aged patients (ages 60 years or older) with MSCC who were operated on with posterior decompressive surgery and spine stabilization were retrospectively analyzed in this study at the Affiliated Hospital of Academy of Military Medical Sciences, Beijing, between 2011 and 2015. The diagnosis of bone metastasis was confirmed histologically, and with adequate diagnostic imaging including spinal CT or MRI, as well as with a bone scan. The data were collected from patients, their family members, treating surgeons, and from patient files. The Medical Research Ethics Board of the Affiliated Hospital of Academy of Military Medical Sciences approved this retrospective study and required neither patient approval nor informed consent for the review of patient images and medical records. The data were retrospective in nature and anonymized by the Medical Research Ethics Board.

We retrospectively analyzed eleven preoperative characteristics for postoperative survival and function outcome, including gender (female *vs*. male), primary site (slow growth *vs*. moderate growth *vs*. rapid growth), preoperative ambulatory status (ambulatory *vs*. not ambulatory), Eastern Cooperative Oncology Group (ECOG) performance status (1-2 *vs*. 3-4), number of involved vertebrae (1-2 *vs*. ≥3, conformed to previous studies), visceral metastases (no *vs*. yes), preoperative chemotherapy (no *vs*. yes), bone metastasis at cancer diagnosis (no *vs*. yes), the time developing motor deficits (≤14 days *vs*. >14 days, conformed to previous studies), preoperative albumin (≤35 g/l *vs*. >35 g/l, conformed to previous studies), and radical surgery at primary site (no *vs*. yes).

Primary cancer was classified into three groups. First, tumors that exhibited slow growth including hormone-dependent breast cancer, hormone-dependent prostate cancer, thyroid cancer, multiple myeloma, and malignant lymphoma. Second, moderate growth including lung cancer treated with molecularly targeted drugs, hormone-independent breast cancer, hormone-independent prostate cancer, renal cell carcinoma, endometrial cancer, ovarian cancer, and sarcoma. Third, rapid growth including lung cancer without molecularly targeted drugs, colorectal cancer, gastric cancer, pancreatic cancer, esophageal cancer, hepatocellular carcinoma, head and neck cancer, melanoma, malignant thymoma and cancers of unknown origin, which was developed from Katagiri et al. [7] The postoperative survival was defined as the time between the date of surgery and death or the latest follow up, and patients who were alive at the last follow up were censored in the postoperative survival analysis. Postoperative function outcome was graded based on Frankel grades preoperatively and about 4 weeks postoperatively (patients with Frankel D and E have the ability to walk). Time to development of 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. Surgery-related complications were recorded with 4 weeks. 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.

The indication for surgery was a neurological deficit due to spinal cord compression. Patients were operated on with posterior decompressive surgery and spine stabilization. Local radiotherapy, systemic chemotherapy, endocrine therapy, or targeted therapy were routinely performed after the wound healed, about 3-4 weeks after the surgery, if applicable.

The Kaplan-Meier method was used to evaluate postoperative survival. Univariate and multivariate analysis of postoperative survival were estimated by the simple and multiple Cox proportional hazards regression models, respectively. Logistic regression model was used to analyze the univariate and multivariate analysis of postoperative function outcome (ambulatory=0, not ambulatory=1). Kappa test, Wilcoxon rank test or Kruskal-Wallis rank test, and a Chi-square test were performed to analyze function outcome after surgery. A *P* value of 0.05 or less was considered statistically significant. Statistical analysis was performed using SAS 9.2 software.

Results

Patient characteristics

In the entire cohort of 54 patients, there were 9 patients with slow growth cancer, 13 patients with moderate growth cancer, and 32 patients with rapid growth cancer (**Table 1**). The median

Table 1. The primary cancer sites in the entire cohort of 54 aged patients with MSCC

Primary site	No. of patients
Slow growth	9
Hormone-dependent breast cancer	3
Hormone-dependent prostate cancer	4
Thyroid cancer	2
Moderate growth	13
Lung cancer treated with molecularly targeted drugs	9
Hormone-independent breast cancer	3
Hormone-independent prostate cancer	1
Rapid growth	32
Lung cancer without molecularly targeted drugs	17
Colorectal cancer	2
Pancreatic cancer	1
Esophageal cancer	5
Urological cancers (except renal cell cancer)	2
Head and neck cancer	2
Cancers of unknown	3

Abbreviations: MSCC, metastatic spinal cord compression.

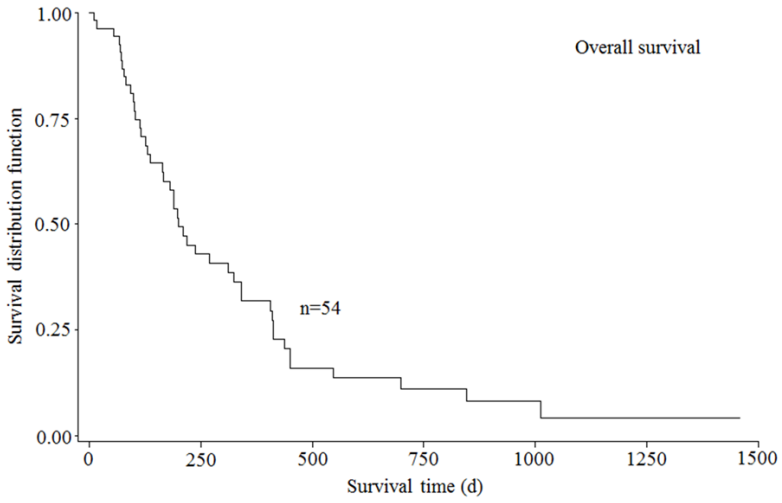

Figure 1. Kaplan-Meier survival curves of postoperative overall survival for aged patients with metastatic spinal cord compression.

overall survival was 6.6 months (95% CI, 4.5-10.8 months), and 6-month and 12-month survival rates were 57.9% and 31.8%, respectively (**Figure 1**). At the latest follow up, seven patients were alive with a mean follow-up of 10.7 months (range, 2.3-48.6 months).

Prognostic factors

In univariate analysis, primary site (HR, 2.01, 95% CI: 1.32-3.06; P<0.01), visceral metastases (HR, 3.31, 95% CI: 1.72-6.36; P<0.01), and radical surgery at primary site (HR, 2.09, 95% CI: 1.07-4.07, P=0.03) were significantly associated with postoperative survival (**Figure 2**). According to the multiple Cox proportional hazards regression model, two of the above four factors, primary site (HR, 2.33, 95% CI: 1.50-3.62; P<0.01) and visceral metastases (HR, 4.58, 95% CI: 2.21-9.48, P<0.01) maintained significant impact on postoperative survival (**Table 2**). In univariate analysis of postoperative function outcome, only visceral metastases (OR, 4.36, 95% CI: 1.17-16.23; P=0.03) were significant, while visceral metastases (OR, 6.41, 95% CI: 1.43-28.77; P=0.02) and preoperative ambulatory status (OR, 4.98, 95% CI: 1.10-22.55; P=0.04) were significantly associated with postoperative function outcome based on multivariate analysis (**Table 3**).

Function outcome

The distribution of pre-operative and post-operative Frankel grades is shown in **Table 4**. There was no significant consistency between the distributions of Frankel grades before surgery and those after surgery (P=0.20), which suggests that decompressive surgery could change the function outcome in aged patients with MSCC. Although there was no significant difference in ambulatory status between pre- and post-operation (P=0.29), the distribution of the total of Frankel grades after surgery was significantly different as compared with those before surgery (P=0.01). In the entire cohort of 54 patients, 83.3% (30/36) of patients maintained their ambulatory status, 61.1% (11/18) of non-ambulatory patients before operation regained the ability to walk, and 75.9% (41/54) of patients were ambulatory after surgery.

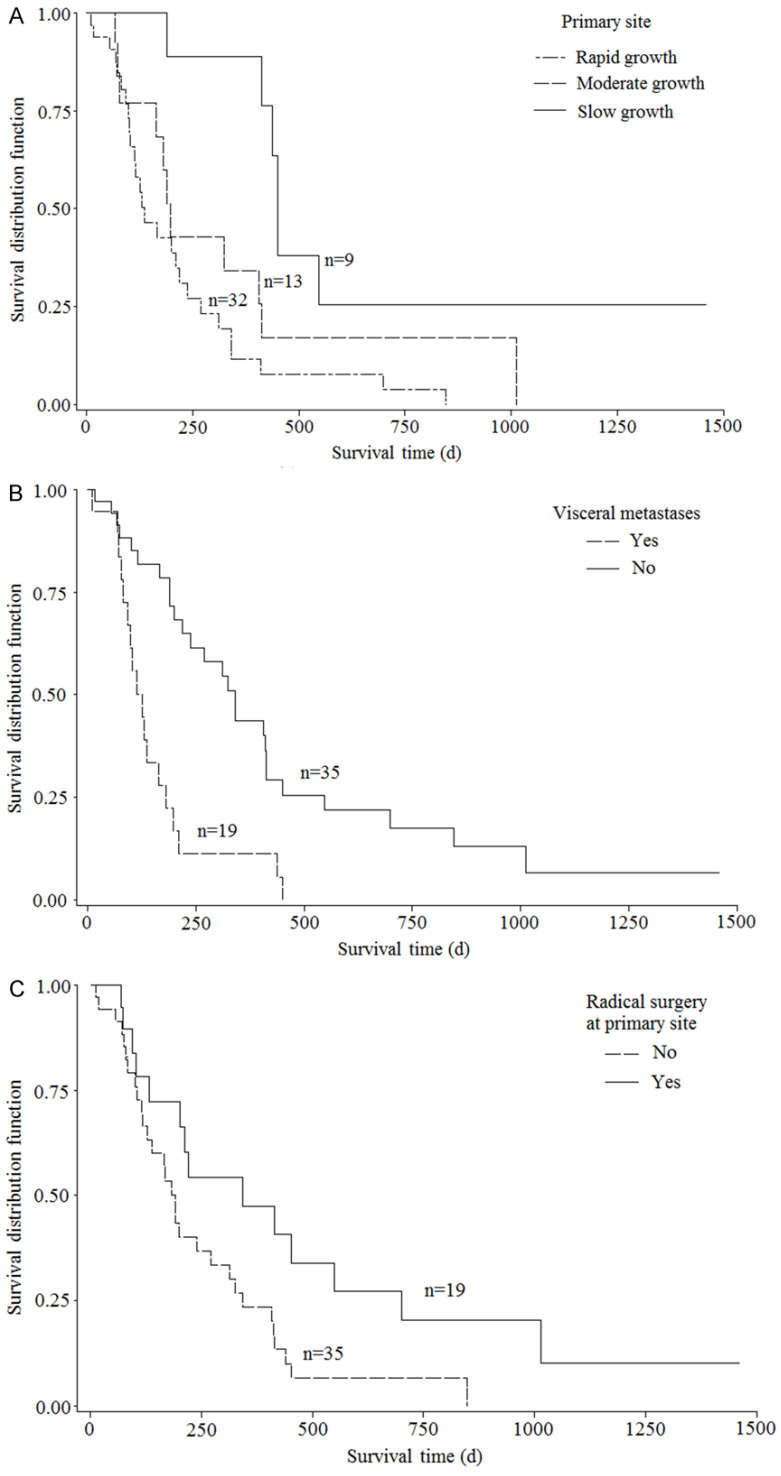

Figure 2. Kaplan-Meier survival curves for preoperative factors in aged patients with metastatic spinal cord compression after decompressive surgery: (A) primary site, (B) visceral metastases, and (C) radical surgery at primary site.

Complications

Eighteen complications occurred within four weeks of surgery in 15 of the 54 patients. Local complications were observed in 5 patients, systemic complications in 7 patients, and 3 patients had both local and systemic complications. More details are shown in **Table 5**. Patients with postoperative complications (4.2 months; 95% CI, 2.3-6.6 months) were found to have a shorter median survival than those who did not (10.4 months; 95% CI, 6.0-13.7 months) (*P*=0.01).

Discussion

The most appropriate treatments for patients with MSCC are still being debated. In 2005, a prospective randomized trial strongly showed that decompressive surgery followed by radiotherapy was superior to radiotherapy alone [8], while a matched pair analysis did not find any benefit of surgery followed by radiotherapy compared with radiotherapy alone, in 2010 [9]. More recently, a 2014 meta-analysis indicated that direct decompressive surgery followed by radiotherapy may produce better clinical improvement of ambulation status and survival than radiotherapy alone [10]. Notably, aged patients with MSCC were not excluded in the above mentioned studies. Generally, direct decompressive surgery has become the standard treatment for selected patients with MSCC, including aged patients with MSCC.

A particular focus has been placed on aged patients, who were usually defined as 60 years or older, since the number of this group in oncology has grown remarkably due to the development of modern medicine, such as targeted therapies [1, 3, 11]. Previously, we

Table 2. Univariate and multivariate analysis of preoperative characteristics for postoperative survival in aged patients with MSCC

Characteristics	Patients (n)	MOS (m)	Simple Cox regression		Multiple Cox regression	
			HR (95% CI)	*P*	HR (95% CI)	*P*
Gender						
Female	25	6.3	0.79 (0.44-1.45)	0.45	Not included	
Male	29	10.4				
Primary site						
Slow growth	9	15.0	2.01 (1.32-3.06)	<0.01	2.33 (1.50-3.62)	<0.01
Moderate growth	13	6.6				
Rapid growth	32	4.5				
Preoperative ambulatory status						
Ambulatory	36	6.6	1.15 (0.62-2.14)	0.65	Not included	
Not Ambulatory	18	6.3				
ECOG Performance status						
1-2	29	7.9	1.31 (0.72-2.38)	0.37	Not included	
3-4	25	6.3				
Number of involved vertebrae						
1-2	35	7.9	1.08 (0.57-2.02)	0.82	Not included	
≥3	19	5.5				
Visceral metastases						
No	35	11.4	3.31 (1.72-6.36)	<0.01	4.58 (2.21-9.48)	<0.01
Yes	19	4.2				
Preoperative chemotherapy						
No	36	6.3	1.87 (0.96-3.66)	0.07	Not included	
Yes	18	13.6				
Bone metastasis at cancer diagnosis						
No	29	7.0	1.59 (0.86-2.94)	0.14	Not included	
Yes	25	6.3				
Time developing motor deficits						
≤14 days	25	6.0	1.35 (0.74-2.46)	0.33	Not included	
>14 days	29	7.3				
Preoperative albumin						
≤35 g/l	21	6.3	1.43 (0.77-2.63)	0.26	Not included	
>35 g/l	33	7.0				
Radical surgery at primary site						
No	35	6.3	2.09 (1.07-4.07)	0.03	Not included	
Yes	19	11.4				

Abbreviations: MSCC, metastatic spinal cord compression; MOS, median overall survival; m, months; HR, hazard ratio; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group.

proposed a scoring system to enable physicians to identify the appropriate candidates for decompression and stabilization in patients with MSCC [12]. However, this score was particularly for non-small cell lung cancer patients, making it not useful for drawing conclusions, especially on aged patients with MSCC. Fortunately, several prognostic factors and scoring systems have been proposed to achieve individualized treatments especially for elderly patients with MSCC. Rades et al. [11, 13, 14] developed new instruments for estimation of survival in aged patients irradiated for MSCC from various primary sites or particularly from

Table 3. Univariate and multivariate analysis of preoperative characteristics for postoperative function outcome in aged patients with MSCC

Characteristics	Ambulatory		Univariate analysis		Multivariate analysis	
	Yes	No	OR (95% CI)	*P*	OR (95% CI)	*P*
Gender						
Female	17	8	0.44 (0.12-1.59)	0.21	Not included	
Male	24	5				
Primary site						
Slow growth	8	1	2.80 (0.88-8.87)	0.08	Not included	
Moderate growth	12	1				
Rapid growth	21	11				
Preoperative ambulatory status						
Ambulatory	30	6	3.18 (0.88-11.57)	0.08	4.98 (1.10-22.55)	0.04
Not Ambulatory	11	7				
ECOG performance status						
1-2	24	5	2.26 (0.63-8.11)	0.21	Not included	
3-4	17	8				
Number of involved vertebrae						
1-2	28	7	1.85 (0.52-6.60)	0.35	Not included	
≥3	13	6				
Visceral metastases						
No	30	5	4.36 (1.17-16.23)	0.03	6.41 (1.43-28.77)	
Yes	11	8				
Preoperative chemotherapy						
No	28	8	0.74 (0.20-2.72)	0.65	Not included	
Yes	13	5				
Bone metastasis at cancer diagnosis						
No	21	8	0.66 (0.18-2.35)	0.52	Not included	
Yes	20	5				
Time developing motor deficits						
≤14 days	19	6	0.99 (0.28-3.47)	0.99	Not included	
>14 days	22	7				
Preoperative albumin						
≤35 g/l	17	4	0.63 (0.17-2.38)	0.49	Not included	
>35 g/l	24	9				
Radical surgery at primary site						
No	26	9	1.30 (0.34-4.95)	0.70	Not included	
Yes	15	4				

Abbreviations: MSCC, metastatic spinal cord compression; OR, odds ratio; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group.

breast cancer and lung cancer. The scoring system for patients with breast cancer alone included five prognostic factors, including visceral metastases, time developing motor deficits, ambulatory status, number of involved vertebrae, and ECOG performance score. Patients with lung cancer alone included the above four prognostic factors, ECOG performance status, time developing motor deficit, visceral metastases, and ambulatory status. However, participants included in the Rades' studies were treated with radiotherapy alone. Also, function outcome was not considered.

In our present study, we included fifty-four patients with MSCC who were treated with decompressive surgery and spine stabilization. The indication for surgery was neurological defi-

Table 4. Neurological recovery of the aged 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	0	0	0	0	
	B	0	1	2	3	1	7	18
	C	0	1[c]	3	5	2	11	
Ambulatory	D	0	1	5	21	9	36	36
	E	0	0	0	0	0	0	
Total[a]		0	3	10	29	12	39	P_1=0.20
Total[b]			13			41	P_2=0.01	P_3=0.29

[a]Regarding Frankel grades; [b]Regarding ambulatory status (Frankel D/E has the ability to walk). [c]One patient with Frankel B died within 4 weeks postoperatively. 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

Table 5. Complications of surgery for aged patients with MSCC within 4 weeks after operation (patients may have more than one complication)

Complications	Patients (n)	Follow-up after operation
Local complications		
Operation site infection	3	2.3, 3.1, and 6.3 months died
Wound dehiscence	1	10.4 months alive
Cerebrospinal fluid leakage	1	4.2 months died
Epidural hematoma	1	15.0 months died
Sacral pressure sores	2	3.4 and 4.3 months died
Systemic complications		
Pneumonia	3	3.4 months alive, 6.6 and 9.0 months died
Pulmonary embolism	1	4.3 months died
Stroke	1	3.3 months died
Septicemia	2	1.8 and 2.3 months died
Intestinal bleeding	1	4.2 months died
Multiple organ failure	2	16 days and 2.5 months died

Abbreviations: MSCC, metastatic spinal cord compression.

cits. To our knowledge, this is the largest population-based study specifically and systematically addressing the prognostic factors and surgical outcome for aged patients with MSCC after surgery. We found that primary site, visceral metastases, and radical surgery at primary site were significantly associated with postoperative survival in univariate analysis. According to the multiple Cox proportional hazards regression model, two of above four factors, primary site and visceral metastases maintain significant impact on postoperative survival. As for the univariate analysis of the postoperative function outcome, only visceral metastases were significant, while visceral metastases and preoperative ambulatory status were significantly associated with postoperative function outcome based on multivariate analysis. Chi et al. [15] showed that surgery, breast cancer tumor type, and higher Frankel score (patients with Frankel D and E were ambulatory) are significantly predictive of better ambulation outcome.

The median overall survival is 6.6 months in the entire aged patients, and 4.5-10.0 months was reported in other studies [6, 15]. Regarding function outcome, there is no significant consistency between the distributions of Frankel grades before surgery and those after surgery,

which suggests that decompressive surgery could change the function outcome. Function outcome is more favorable after surgery when compared with those before surgery (P=0.01). In the entire cohort of 54 patients, 83.3% (30/36) patients maintained their ambulatory status, 61.1% (11/18) non-ambulatory patients before operation regained the ability to walk, and 75.9% (41/54) patients were ambulatory after surgery. 55%-90% of patients had the ability to walk in other studies [6, 15]. Eighteen complications occurred within four weeks of surgery in 27.8% (15/54) patients, 27%-35% patients experienced surgical complications in other reports [16, 17]. In our series, operation site infection was observed in three cases, which was successfully treated by continuous irrigation combined with antibiotics. Cerebrospinal fluid leakage was found in one case and required percutaneous lumbar drainage. One patient showed epidural hematoma and required surgical removal. One patient who experienced wound dehiscence had received radiation therapy to the operation site 7 days postoperatively. Patients should not receive radiotherapy until the operation wound has healed, preoperative baths for patients are given, and early mobilization which can minimize postoperative complications.

In conclusion, surgical treatment of aged patients with MSCC is found to be effective in terms of neurological recovery with a tolerable rate of complications. Our findings suggest that primary site and visceral metastases are significantly associated with postoperative survival. Visceral metastases and preoperative ambulatory status are independent prognostic factors for postoperative function outcome. Those factors can help select the individual treatment, especially for aged patients with MSCC. For patients with slow growth cancer, ambulatory, and no visceral metastases surgery should be adopted. However, great care should be taken in cases with rapid growth cancer, non-ambulatory, and visceral metastases. Importantly, visceral metastases should always be carefully evaluated because this factor is found to be related to both postoperative survival and function outcome. Nevertheless, a larger prospective study is still needed.

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Disclosure of conflict of interest

None.

Abbreviations

MSCC, metastatic spinal cord compression; MOS, median overall survival; m, months; HR, hazard ratio; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group.

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