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Original Article

What are the differences in clinical outcomes between the older and the younger patients with metastatic epidural spinal cord compression after decompressive surgery? A systematic comparison

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Abstract: This study aims to systematically compare the surgical results and prognostic factors between the older and the younger patients after decompressive surgery for metastatic epidural spinal cord compression (MESCC). Fifty-four older patients and sixty-five relatively younger patients with MESCC who were operated with decompressive surgery and spine stabilization were retrospectively analyzed in this study. Postoperative survival time, ambulatory outcome, and surgery-related complications were compared between the two groups. Besides, we retrospectively analyzed eleven preoperative characteristics for postoperative ambulatory outcome in both groups. The younger group (10.2 months, 95% CI, 6.2-12.8 months) had a relatively longer median overall survival than the older group (6.6 months, 95% CI, 4.5-10.8 months), but it reached no significance (P=0.24). The median overall ambulatory time of the older and younger groups was 3.7 months (95% CI, 3.0-6.6 months) and 6.0 months (95% CI, 3.7-8.6 months), respectively (P=0.03). In the multivariate analysis, primary site (P<0.01), preoperative ambulatory status (P<0.01) and visceral metastases (P<0.01) were significant associated with postoperative ambulatory outcome in the older group, while preoperative ambulatory status (P=0.01), preoperative chemotherapy (P=0.02), time developing motor deficits (P=0.03), and radical surgery at primary site (P<0.01) were found to be significantly independent prognostic factors in the younger group. Surgery-related complications occurred in 27.8% patients in the older group and 10.8% patients in the younger group (P=0.02). MESCC in the older patients had a poorer ambulatory outcome and a relative higher surgery-related complication as compared with MESCC in the younger patients. Primary site, preoperative ambulatory status and visceral metastases were independent prognostic factors for postoperative ambulatory outcome especially in the older patients with MESCC. Preoperative ambulatory status, preoperative chemotherapy, time developing motor deficits, and radical surgery at primary site were independent predictive factors in the younger patients with MESCC.

Keywords: Older patients, younger patients, metastatic epidural spinal cord compression, surgical decompression and spine stabilization, ambulatory outcome

Introduction

Metastatic epidural spinal cord compression (MESCC), a common and debilitating complication of advanced cancers, is considered an oncologic emergency that can result in irreversible loss of neurologic function if left untreated, negatively affecting the patents' quality of remaining life [1]. Patients who die from cancers have an estimated 3.4% annual incidence of MESCC and require hospitalization [2]. Notably, the situation is somewhat more complicated in older patients with MESCC because those patients usually have a poor tolerance to treatment, worse immune system, age-related general disease, and relatively shorter life expectancy, which present challenges for surgeons to make a surgical decision. Moreover, surgery-related complications, especially serious cardiovascular and other systemic complications, occur more frequently in older patients [3, 4]. Thus, the primary goal in treating the older patients is to preserve or improve overall quality of their remaining life and do less harm.

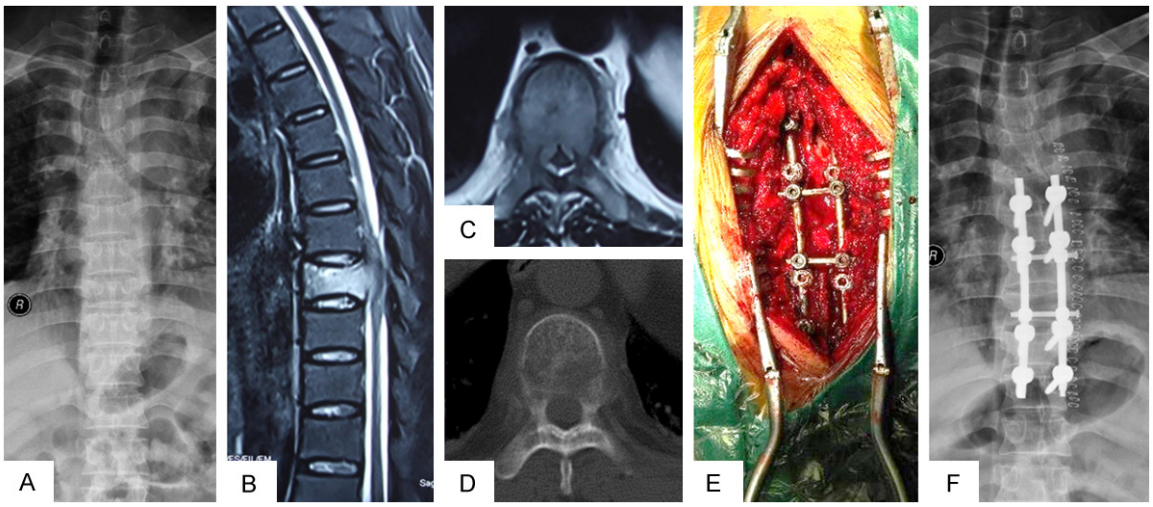

Figure 1. A 62-year-old man who was unable to walk due to metastatic spinal cord compression (MESCC) resulted from lung cancer. A. Preoperative X-ray presented vertebral collapse at T8. B. Preoperative MRI showed spinal cord compression at T8. C. Preoperative MRI showed spinal cord compression at T8. D. Preoperative CT showed bone destruction at T8. E. Intra-operation. F. Following laminectomy at T7 and T8, and pedicle screw fixation was conducted to spine stabilization.

With careful patient selection, long duration of ambulation in aged patients with MESCC can be achieved by surgery, which would remarkably improve patients' quality of remaining life [5]. Besides, more radical procedures, such as total en bloc spondylectomy, should not be avoided due to advanced patient age [3]. Unfortunately, the selection criteria of the surgery in older patients still remains controversial. Individual therapy is needed to avoid surgical treatment on those who are likely to die soon and should take into account postoperative survival prognosis and function outcome [6], which can be estimated by prognostic factors. Surgical outcome and prognostic factors are somewhat different between the older and the younger patients, while there is no study systematically compared the surgical results and prognostic factors between the older and the younger patients with MESCC.

Therefore, in the present study, postoperative survival time, ambulatory outcome, and surgery-related complications were carefully compared between the older and the younger patients with MESCC. Besides, we retrospectively analyzed eleven preoperative characteristics for postoperative ambulatory outcome in the older and the younger groups.

Patients and methods

Fifty-four aged patients (age: 60 years old or older) and sixty-five relatively younger patients (age: 59 years old or younger) with MESCC were retrospectively analyzed in the study at the Affiliated Hospital of Academy of Military Medical Sciences, Beijing, between January 2011 and September 2015. Patients were operated with decompressive surgery and spine stabilization (Case report was shown in **Figure 1**). The indication for surgery was neurological deficit due to spinal cord compression resulted from spine bone metastasis. The diagnosis of bone metastasis was histologically confirmed, and MESCC was confirmed by MRI. Local radiotherapy, systemic chemotherapy, or endocrine therapy were routinely performed after the wound healed, about 3-4 weeks after the surgery, if applicable. Patients with very poor expected survival prognosis who were too poor to undergo surgery were excluded. This retrospective study was approved by the Medical Research Ethics Board of the Affiliated Hospital of Academy of Military Medical Sciences.

We systematically analyzed postoperative survival, ambulatory outcome, and surgery-related complications between the older and younger groups. Besides, eleven preoperative characteristics for postoperative ambulatory outcome were also evaluated in both groups, 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),

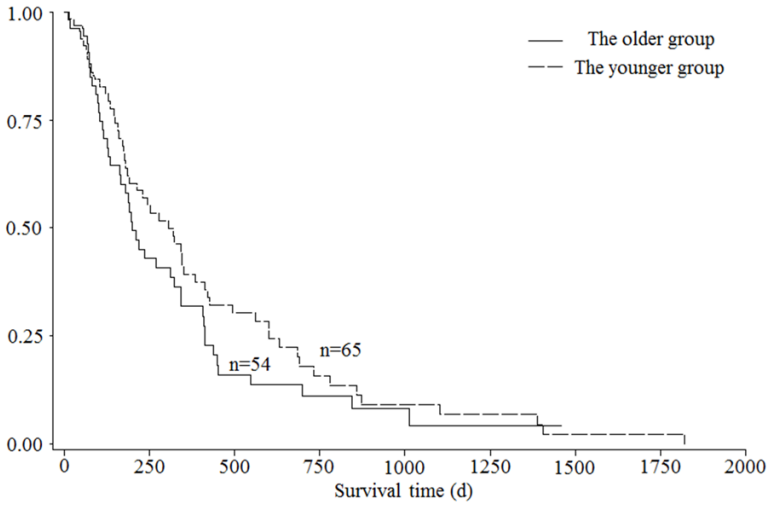

Figure 2. Kaplan-Meier survival curves for postoperative overall survival in the older and the younger groups (P=0.24, log-rank test).

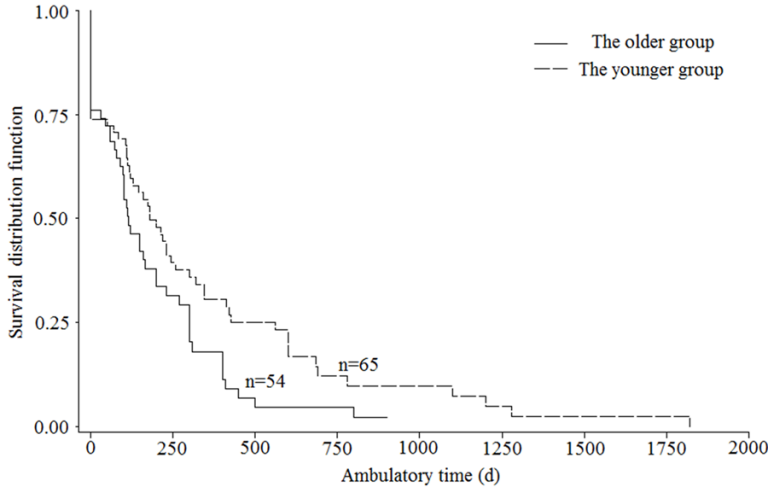

Figure 3. Kaplan-Meier survival curves for postoperative ambulatory time in the older and the younger groups (P=0.03, log-rank test).

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, namely, tumors that exhibited slow growth, moderate growth, or rapid growth, 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. 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. Postoperative ambulatory time was defined as the time between the date of regaining ambulatory status and the date of losing ambulatory status after surgery or the last follow-up. Postoperative ambulatory time was the measurement of postoperative ambulatory outcome. Surgery-related complications were recorded intraoperatively or within 4 weeks postoperatively.

Statistical analysis was performed using SAS 9.2 (SAS Institute Inc., Cary, NC), and the significance level was set at P<0.05. The Kaplan-Meier method and log-rank test was used to evaluate postoperative survival and ambulatory time. The univariate and multivariate analysis of postoperative ambulatory outcome were estimated by the simple and multiple Cox proportional hazards regression models, respectively. Chi-square test were performed to analyze postoperative ambulatory status and surgery-related complications in both groups. Regression model was also used to identify the difference in key complications between older and younger.

Results

The median overall survival of the older and younger groups was 6.6 months (95% CI, 4.5-

Table 1. Univariate and multivariate analysis of preoperative characteristics for postoperative ambulatory outcome in older patients with MESCC

Characteristics	Patients (n)	MOA (m)	Simple Cox regression		Multiple Cox regression	
			HR (95% CI)	*P*	HR (95% CI)	P
Gender						
Female	25	100	0.81 (0.45-1.43)	0.46	Not included	
Male	29	120				
Primary site						
Slow growth	9	300	1.86 (1.22-2.84)	<0.01	1.92 (1.23-2.98)	<0.01
Moderate growth	13	160				
Rapid growth	32	90				
Preoperative ambulatory status						
Ambulatory	36	167	2.20 (1.20-4.01)	0.01	2.26 (1.22-4.20)	<0.01
Not Ambulatory	18	53				
ECOG performance status						
1-2	29	199	1.86 (1.04-3.33)	0.04	Not included	
3-4	25	90				
Number of involved vertebrae						
1-2	35	120	1.19 (0.65-2.15)	0.58	Not included	
≥3	19	100				
Visceral metastases						
No	35	199	3.08 (1.60-5.95)	<0.01	4.16 (2.02-8.57)	<0.01
Yes	19	60				
Preoperative chemotherapy						
No	36	120	1.18 (0.64-2.19)	0.60	Not included	
Yes	18	90				
Bone metastasis at cancer diagnosis						
No	29	110	1.04 (0.58-1.86)	0.91	Not included	
Yes	25	120				
Time developing motor deficits						
≤14 days	25	120	1.23 (0.69-2.19)	0.49	Not included	
>14 days	29	112				
Preoperative albumin						
≤35 g/l	21	112	1.22 (0.67-2.23)	0.51	Not included	
>35 g/l	33	160				
Radical surgery at primary site						
No	35	112	1.53 (0.82-2.86)	0.18	Not included	
Yes	19	199				

Abbreviations: MESCC, Metastatic epidural spinal cord compression; MOA, median overall ambulatory time; m, months; HR, hazard ratio; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group. Excluded criteria: (1) patients with age less than 60 years old; (2) patients without neurological deficit; (3) health was too poor to undergo surgery; (4) intradural metastases; (5) pathological fracture in the lower limbs.

10.8 months) and 10.2 months (95% CI, 6.2-12.8 months), respectively. The younger group had a relatively longer median overall survival than the older group, but it reached no significance (P=0.24, **Figure 2**). The corresponding 6-months survival rates of both groups were 57.9% and 63.8%, respectively, and the 12-months survival rates were 31.8% and 39.2%, respectively. At the latest follow up, seven patients were alive with a mean follow-up of 10.7 months (range, 2.3-48.6 months) in the older group, and nine patients with a mean follow-up of 9.2 months (range, 2.1-22.1 months) in the younger group.

Table 2. Univariate and multivariate analysis of preoperative characteristics for postoperative ambulatory outcome in younger patients with MESCC

Characteristics	Patients (n)	MOA (m)	Univariate analysis		Multivariate analysis	
			HR (95% CI)	*P*	HR (95% CI)	*P*
Gender						
Female	33	245	1.80 (1.05-3.09)	0.03	Not included	
Male	32	120				
Primary site						
Slow growth	14	426	1.58 (1.11-2.25)	0.01	Not included	
Moderate growth	19	245				
Rapid growth	32	119				
Preoperative ambulatory status						
Ambulatory	33	321	2.10 (1.22-3.62)	<0.01	2.10 (1.19-3.71)	0.01
Not Ambulatory	32	97				
ECOG performance status						
1-2	29	321	1.78 (1.03-3.09)	0.04	Not included	
3-4	36	145				
Number of involved vertebrae						
1-2	34	200	1.10 (0.65-1.86)	0.73	Not included	
≥3	31	173				
Visceral metastases						
No	35	321	1.74 (1.02-2.96)	0.04	Not included	
Yes	30	95				
Preoperative chemotherapy						
No	33	120	2.37 (1.33-4.24)	<0.01	2.11 (1.13-3.95)	0.02
Yes	32	321				
Bone metastasis at cancer diagnosis						
No	33	245	1.93 (1.10-3.39)	0.02	Not included	
Yes	32	119				
Time developing motor deficits						
≤14 days	34	120	1.71 (1.00-2.93)	0.05	1.85 (1.05-3.25)	0.03
>14 days	31	346				
Preoperative albumin						
≤35 g/l	25	212	0.90 (0.53-1.56)	0.72	Not included	
>35 g/l	40	173				
Radical surgery at primary site						
No	37	119	2.58 (1.41-4.73)	<0.01	2.37 (1.24-4.52)	<0.01
Yes	28	257				

Abbreviations: MESCC, Metastatic epidural spinal cord compression; MOA, median overall ambulatory time; m, months; HR, hazard ratio; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group. Excluded criteria: (1) patients with age more than 59 years old; (2) patients without neurological deficit; (3) health was too poor to undergo surgery; (4) intradural metastases; (5) pathological fracture in the lower limbs.

Regarding ambulatory outcome, the median overall ambulatory time of the older and the younger groups was 3.7 months (95% CI, 3.0-6.6 months) and 6.0 months (95% CI, 3.7-8.6 months), respectively (P=0.03, **Figure 3**).

In the univariate analysis of the older group, we found primary site (HR, 1.86, 95% CI: 1.22-2.84; P<0.01), preoperative ambulatory status (HR, 2.20, 95% CI: 1.20-4.01; P=0.01), ECOG performance status (HR, 1.86, 95% CI: 1.04-3.33; P=0.04), and visceral metastases (HR, 3.08, 95% CI: 1.60-5.95; P<0.01) were significantly associated with postoperative ambulatory outcome (**Table 1**). According to the multiple Cox proportional hazards regression model,

Table 3. Neurological recovery and complications of the older and younger groups

Groups		Patients (n)	Neurological status[1]		Chi square value	P[2]	Complications[3]		Chi square value	P[4]
			Ambulatory	Nonambulatory			Yes	No		
Older	Pre-	54	36	18	1.13	0.29	15	39	5.66	0.02
	Post-		41	13						
Younger	Pre-	65	33	32	7.37	<0.01	7	58		
	Post-		48	17						

[1]Four weeks postoperatively. [2]*P* value for pre- and postoperative comparison. [3]Within four weeks. [4]*P* value for the older and younger comparison. Abbreviations: Pre-, preoperative; Post-, postoperative.

Table 4. Complications of surgery for the older and the younger patients with MESCC within 4 weeks after operation (patients may have more than one complication)

Complications	The older group (n=54)	The younger group (n=65)
Local complications		
Operation site infection	3 (5.6%)	1 (1.5%)
Wound dehiscence	1 (1.9%)	1 (1.5%)
Cerebrospinal fluid leakage	1 (1.9%)	1 (1.5%)
epidural hematoma	1 (1.9%)	1 (1.5%)
Sacral pressure sores	2 (3.7%)	0 (0)
Systemic complications		
Pneumonia	3 (5.6%)	0 (0)
Pulmonary embolism	1 (1.9%)	0 (0)
Stroke	1 (1.9%)	0 (0)
Septicemia	2 (3.7%)	1 (1.5%)
Intestinal bleeding	1 (1.9%)	2 (3.1%)
Multiple organ failure	2 (3.7%)	1 (1.5%)
Total (%)	18 (33.7%)	8 (12.1%)
P (Chi square value)	<0.01 (7.64)	

Abbreviations: MESCC, Metastatic epidural spinal cord compression.

three of above four factors, primary site (HR, 1.92, 95% CI: 1.23-2.98; P<0.01), preoperative ambulatory status (HR, 2.26, 95% CI: 1.22-4.20; P<0.01) and visceral metastases (HR, 4.16, 95% CI: 2.02-8.57; P<0.01) maintained significance. In the younger group, gender (HR, 1.80, 95% CI: 1.05-3.09; P=0.03), primary site (HR, 1.58, 95% CI: 1.11-2.25; P=0.01), preoperative ambulatory status (HR, 2.10, 95% CI: 1.22-3.62; P<0.01), ECOG performance status (HR, 1.78, 95% CI: 1.03-3.09; P=0.04), visceral metastases (HR, 1.74, 95% CI: 1.02-2.96; P=0.04), preoperative chemotherapy (HR, 2.37, 95% CI: 1.33-4.24; P<0.01), bone metastasis at cancer diagnosis (HR, 1.93, 95% CI: 1.10-3.39; P=0.02), and radical surgery at primary site (HR, 2.58, 95% CI: 1.41-4.73; P<0.01) were significant in the univariate analysis (**Table 2**). However, in the multivariate analysis, preoperative ambulatory status (HR, 2.10, 95% CI: 1.19-3.71; P=0.01), preoperative chemotherapy (HR, 2.11, 95% CI: 1.13-3.95; P=0.02), time developing motor deficits (HR, 1.85, 95% CI: 1.05-3.25, P=0.03), and radical surgery at primary site (HR, 2.37, 95% CI: 1.24-4.52; P<0.01) had significant impact on postoperative ambulatory outcome.

The ambulatory rate of the older group showed no difference before and after surgery (P=0.29). In details, 66.7% (36/54) patients were ambulatory before surgery and 75.9% (41/54) patients had the ability to walk postoperatively in the older group. However, 50.8% patients were ambulatory before operation and 73.8% patients had the ability to walk postoperatively in the younger group (P<0.01, **Table 3**). Eighteen complications occurred within four weeks of surgery in 15 of the 54 patients in the older group and eight complications were recorded in 7 of the 65 patients in the younger group (P=0.02). As compared with younger patients, older patients with MESCC had higher risk of suffering from surgery-related complications (odds ratio, 2.01; 95% CI: 0.76-5.38, P=0.16), but it didn't reach significance. More details were shown in **Table 4**.

Discussion

In the present study, we systematically compared the postoperative survival time, ambulatory outcome, and surgery-related complications between the older and the younger patients with MESCC. A multicenter prospective study strongly showed that survival expectancy was significantly longer in relatively younger patients in a series of 1266 patients with spine metastasis or MESCC [8]. The young-

er group (10.2 months) had a relatively longer median overall survival than the older group (6.6 months), but it reached no significance in our study. Regarding ambulatory outcome, the median overall ambulatory time of the older and the younger groups was 3.7 months (95% CI, 3.0-6.6 months) and 6.0 months (95% CI, 3.7-8.6 months), respectively (P=0.03), which suggested that the younger group had a better postoperative ambulatory outcome as compared with the older group. Similar results were reported in other studies [8, 9].

Several studies have shown that the primary tumor histology, preoperative Frankel grades, and Tokuhashi scores in MESCC patients were the important prognostic factors for survival [8, 10-13]. Previously, we also proposed scoring systems to enable physicians to select appropriate treatments for MESCC patients depending on their survival and functional prognosis [14-16]. However, those papers were not especially for aged patients with MESCC. Besides, there was few article addressing the predictive factors for postoperative ambulatory outcome in MESCC patients. Notably, function outcome after surgery plays an important role in patient's quality of remaining life [8, 17]. In the present study, we found primary site, preoperative ambulatory status, ECOG performance status, and visceral metastases were significantly associated with postoperative ambulatory outcome in the univariate analysis of the older group. According to the multiple Cox proportional hazards regression model, three of above four factors, primary site, preoperative ambulatory status and visceral metastases maintained significance. In the younger group, gender, primary site, preoperative ambulatory status, ECOG performance status, visceral metastases, preoperative chemotherapy, bone metastasis at cancer diagnosis, and radical surgery at primary site were significant in the univariate analysis. However, in the multivariate analysis, preoperative ambulatory status, preoperative chemotherapy, time developing motor deficits, and radical surgery at primary site had significant impact on postoperative ambulatory outcome. Thus, the younger patients with MESCC may benefit more from preoperative chemotherapy and radical surgery at primary site, since they often had better general status and stronger tolerance to those treatments. Primary site, preoperative ambulatory status and visceral metastases were independent prognostic factors for postoperative ambulatory outcome especially in the older patients with MESCC, which indicated the older patients with rapid growth tumor, nonambulatory status and visceral metastases may suffer from worse ambulatory outcome, so surgery should not be considered in those patients. Interestingly, preoperative ambulatory status was significantly associated with ambulatory outcome both in the older and younger groups. Many studies have shown that preoperative ambulatory status was one of the most important predictive factors for postoperative ambulatory status [18-20]. The postoperative complication rate in the older group (27.8%) was significantly higher when compared with the younger group (10.8%, P=0.02), mainly due to increased infection and pulmonary disease. Notably, not all patients who were treated with surgery could experience benefit and the risk of surgical complications, based on other reports, can be as high as 35% [21, 22]. Thus, the above identified prognostic factors may help properly identify appropriate candidates for costly and potentially risky surgery.

In conclusion, MESCC in the older patients had a poorer ambulatory outcome and a relative higher surgery-related complications as compared with MESCC in the younger patients. Primary site, preoperative ambulatory status and visceral metastases were independent prognostic factors for postoperative ambulatory outcome especially in the older group. Preoperative ambulatory status, preoperative chemotherapy, time developing motor deficits, and radical surgery at primary site were predictive factors for postoperative ambulatory outcome in the younger group. Those prognostic factors should be considered to help select the appropriate treatments especially for the older or younger patients with MESCC.

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Disclosure of conflict of interest

None.

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