

Clinical outcomes and risk factors in patients with cervical metastatic spinal cord compression after posterior decompressive and spinal stabilization surgery

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Purpose: The aim of this study was to investigate the clinical results of surgery for cervical spine metastasis and identify clinical risk factors affecting postoperative survival and neurological outcome.

Patients and methods: A retrospective analysis of medical records was performed on 19 patients who had undergone decompressive surgery and spine stabilization due to metastatic spinal cord compression in the cervical spine. All patients had severe pain before surgery. Worst pain, average pain, and pain interference were evaluated using the visual analog scale (range, 0–10) for each patient at baseline and following surgery. Neurological recovery was assessed using the Japanese Orthopaedic Association Score (JOAS). In addition, associations between ten characteristics and postoperative survival and neurological outcomes were analyzed in the study.

Results: The mean worst pain score in a 24-hour period was 8.6 before the operation. At 1 day, 1, 3, 6, and 12 months after the operation, the mean worst pain scores decreased to 5.6, 4.5, 3.8, 2.6, and 2.4 (all $P < 0.001$ vs baseline), respectively. Similar decreases in average pain and pain interference were also observed. The median JOAS in a 24-hour period was 11.0 before the operation. At 1 day, 1, 3, 6, and 12 months after the operation, the median JOAS increased to 12.0 ($P = 0.469$), 13.0 ($P = 0.010$), 14.0 ($P < 0.001$), 15.0 ($P < 0.001$), and 14.0 ($P < 0.001$), respectively. According to the multivariate analysis, postoperative survival was significantly associated with the type of primary tumor ($P = 0.033$), preoperative ambulatory status ($P = 0.004$), extra-spinal bone metastasis ($P = 0.021$), ¹²⁵I seed brachytherapy ($P = 0.014$), and complication status ($P = 0.009$). Better neurological outcome was found to be correlated with higher JOAS ($P = 0.013$). Surgery-related complications occurred in 26.3% of patients.

Conclusion: Posterior decompression and spine stabilization for painful cervical spine metastasis resulting from spinal cord compression were found to be effective for neurological recovery and pain control with a tolerable rate of complications.

Keywords: cervical spine metastasis, surgery, survival prognosis, neurological outcome, visual analog scale, Japanese Orthopaedic Association Score

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Introduction

Cervical spine metastasis is less frequent than metastasis to other parts of the spine.¹ Unfortunately, metastatic disease in the cervical spine can result in severe pain, respiratory failure, and neurological quadriplegia due to metastatic spinal cord compression (MSCC).² MSCC is regarded as an oncologic emergency that occurs in up to 10% of adult patients with cancer during their disease courses and can become

symptomatic, which involves intractable pain, neurological deficits, or even bladder and bowel dysfunction, adversely affecting the patient's quality of life.^{2,3} Treatments for MSCC in the cervical spine include radiotherapy,⁴ vertebroplasty,⁵ surgery,⁶ corticosteroids, and symptom control, alone or in combination, which are effective for improving or maintaining neurological function, relieving pain, stabilizing the spine, and positively improving the patient's quality of life.⁷

In 2005, a phase III trial strongly suggested that direct decompressive surgery following postoperative radiotherapy was superior to treatment with radiotherapy alone for MSCC in terms of ambulatory status, regaining the ability to walk, ambulatory duration, and survival in selected patients. Notably, patients with MSCC in the cervical spine were included in this study.⁸ Therefore, posterior approaches, starting with decompressive laminectomy followed by spine stabilization, have traditionally been the most common surgical procedures for MSCC.

Surgery is technically challenging in the cervical spine due to the complicated anatomy of this region, and metastatic disease in the cervical spine is considered a poorer prognosis than in the thoracic and lumbar spine. Few publications have addressed the surgical results and clinical outcomes of cervical spine metastasis, let alone MSCC in cervical spine treated with posterior decompression and spine stabilization. In this study, pain outcome and neurological recovery were used to evaluate surgical results, and factors for survival and neurological outcomes were also analyzed.

Patients and methods

Nineteen patients with MSCC in the cervical spine who had been operated with decompression and spine stabilization were retrospectively analyzed in our department between May 2013 and May 2017. The indication for surgery was neurological deficit (sensory and/or motor function impairment, sphincter dysfunction) due to MSCC which had been confirmed by spinal magnetic resonance imaging, and a life expectancy of at least 3 months. Surgery was not performed on those whose expected survivals were <3 months and in those whose health was too poor to undergo surgery. That was consistent with the Spine Oncology Study Group.⁹ All patients had severe pain before surgery. The diagnosis of cancer or bone metastasis was confirmed histologically. All the patients were operated with posterior decompression and spine stabilization in our department (Figure 1). Corticosteroids were routinely used before surgery. Local radiotherapy, systemic chemotherapy, and targeted therapy were performed after the wound healed, about 3–4 weeks after the surgery. Patients with missing data were not included. The Medical Research Ethics Board of the Affiliated Hospital of Academy of Military Medical Sciences approved this retrospective study and waived patient consent for review of medical images and records, as all data were anonymized. This study was conducted in accordance with the Declaration of Helsinki.

Visual analog scale (VAS), ranging from 0 to 10, was used to evaluate the worst pain, average pain, and pain

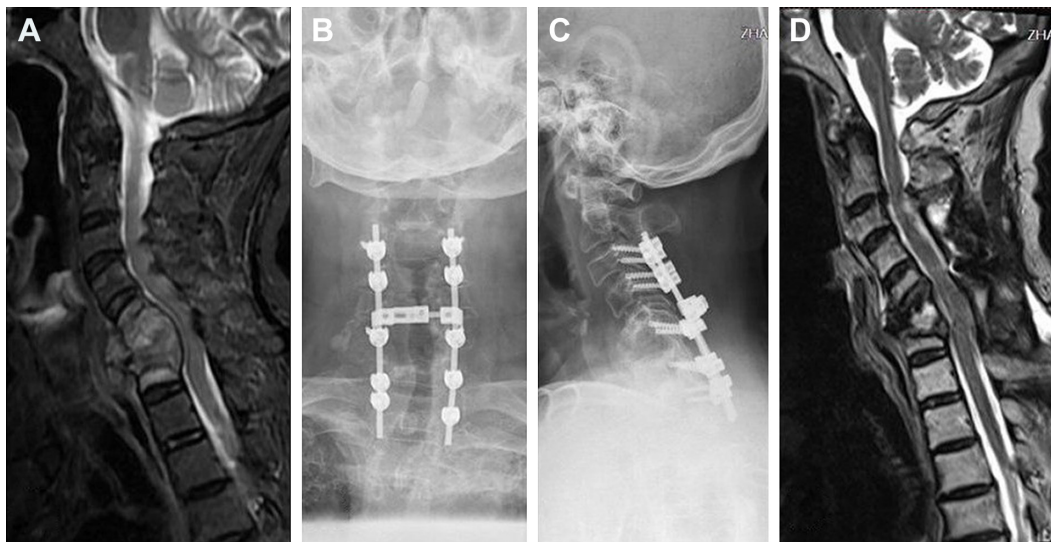


Figure 1 A 45-year-old male was unable to walk due to MSCC resulting from lung cancer.

Notes: (A) Preoperative MRI shows the pathologic collapse of C5 and C6. (B, C) Following laminectomy at C4–C5, lateral mass screws fixation was conducted for spine stabilization. (D) The postoperative MRI showed that the spinal canal was widened and spinal cord compression was removed. Postoperative motor function improved from 12 to 25 points (based on JOAS). The patient died at postoperative 4.1 months and spine stability was maintained throughout the survival period.

Abbreviations: JOAS, Japanese Orthopaedic Association Score; MRI, magnetic resonance imaging; MSCC, metastatic spinal cord compression.

interference for each patient at baseline and following surgery within 24 hours and at 1, 3, 6, and 12 months. Neurological recovery was assessed based on Japanese Orthopaedic Association Score (JOAS; Table 1) within 24 hours before the operation and 24 hours, 1, 3, 6, and 12 months after the operation. In addition, 10 characteristics were analyzed for postoperative neurological and survival outcome. These characteristics included age (≤ 57 years vs > 57 years, median age: 57 years), sex (female vs male), type of primary cancer (slow growth vs rapid growth), ambulatory status (can vs cannot), extra-spinal bone metastasis (no vs yes), visceral metastasis (no vs yes), time for developing motor deficit (≤ 2 weeks vs > 2 weeks), ^{125}I seed brachytherapy (no vs yes), complication (no vs yes), and JOAS (severe: score < 10 vs mild: score ≥ 10). All the above-mentioned characteristics were commonly analyzed in previous studies.

Analysis of the VAS and JOAS in a 24-hour period was performed via repeated measures of the correlated variance model across each time point, supplemented by Wilcoxon

rank-sum test. Univariate and multivariate analyses of the survival outcome were performed with the Kaplan–Meier method and the log-rank test and the multiple Cox regression model, respectively. Both univariate and multivariate analyses of the neurological prognosis were performed with the ordered-logit model. A P -value of ≤ 0.05 was considered statistically significant. Statistical analysis was performed using SAS 9.2 software (SAS Institute Inc, Cary, NC, USA).

Results

Patient characteristics

Patients' demographic data are summarized in Table 2. The median age of the patients (9 females and 10 males) was 51 years (range: 29–69 years). Cases were classified into two groups according to primary tumor's growth rate. The slow growth group included breast cancer (four cases), thyroid cancer (three cases), and renal cancer (one case) while the rapid growth group included lung cancer (eight cases), esophagus cancer, colorectal cancer, and unknown original cancer site (one case each). The involved levels were C1 in one case (5%), C2 in three cases (16%), C3 in three cases (16%), C4 in four cases (21%), C5 in five cases (26%), C6 in seven cases (37%), and C7 in seven cases (37%), which showed low incidence in the upper cervical spine. The median length of follow-up was 10 months (range: 3–18 months).

Surgical results

The mean worst pain score in a 24-hour period was 8.6 before the operation. At 1 day, 1, 3, 6, and 12 months after the operation, the mean worst pain scores decreased to 5.6, 4.5, 3.8, 2.6, and 2.4, respectively (all $P < 0.001$ vs baseline; Table 3, Figure 2). Similar decreases in average pain and pain interference were observed. In detail, the worst pain relief (a 2-score drop in pain was defined as clinically significant relief) was observed in 78.9% of the patients, average pain relief was achieved in 89.5% of the patients, and pain interference relief occurred in 84.2% of the patients after surgery. The median JOAS in a 24-hour period was 11.0 before the operation. At 1 day, 1, 3, 6, and 12 months after the operation, the median JOAS increased to 12.0 ($P = 0.469$), 13.0 ($P = 0.010$), 14.0 ($P < 0.001$), 15.0 ($P < 0.001$), and 14.0 ($P < 0.001$), respectively.

Clinical outcomes

In the entire cohort of 19 patients, the overall median survival time was 11.5 months; 6-month and 12-month survival rates were 73.7% and 46.3%, respectively. According to the univariate analysis, factors that were found to be related

Table 1 Neurological function as determined using the JOAS system

Contents	Score
Motor dysfunction score of the upper extremities	
Unable to feed oneself	0
Unable to handle chopsticks, able to eat with spoon	1
Handled chopsticks with much difficulty	2
Handled chopsticks with slight difficulty	3
None	4
Motor dysfunction score of the lower extremities	
Unable to walk	0
Walk with walking aid	1
Able to go up and/or downstairs with handrail for support	2
Lack of stability and smooth gait	3
None	4
Sensory deficits	
A) Upper extremities	
Severe sensory loss or pain	0
Mild sensory loss	1
None	2
B) Lower extremities same as A	
C) Trunk same as A	
Sphincter dysfunction	
Unable to void	0
Marked difficulty in micturition (retention, strangury)	1
Difficulty in micturition (pollakisuria, hesitation)	2
None	3
Total (maximum score)	17

Abbreviation: JOAS, Japanese Orthopaedic Association Score.

Table 2 Demographic and clinical characteristics of 19 patients who underwent decompression and spine stabilization for MSCC in the cervical spine

Case	Age, years	Sex	Primary cancer	Involved level	Ambulatory status	Extra-spinal BM	Visceral metastasis	¹²⁵ I seed	Motor deficit time (days)	JOAS (0–17)	Complication
1	45	F	Lung	C5, C6	Cannot	Femur	No	Yes	15	11	No
2	42	M	Lung	C7, T1	Can	Femur	Brain	No	3	7	No
3	46	F	Breast	C6	Cannot	No	No	No	22	12	No
4	45	M	Lung	C5, C6	Cannot	Ilium, sacrum, rib	No	No	25	12	Infection
5	51	M	Thyroid	C4	Can	Sternum, rib	Lung	Yes	19	16	No
6	58	F	Breast	C7–T2	Can	No	No	Yes	17	14	No
7	51	F	Thyroid	C5–C7	Can	Femur	No	Yes	21	16	No
8	58	M	Lung	C5, C6	Cannot	Sternum, femur	No	Yes	12	10	No
9	58	F	Esophagus	C5	Cannot	No	Liver, pancreas	No	7	8	Pneumonia
10	51	F	Lung	C3, C4	Can	Rib, sternum	No	No	56	6	Infection
11	29	M	Colorectal	C6, C7	Cannot	Ilium	Liver	No	10	5	No
12	47	M	Lung	C1–3	Can	Humerus, ilium	No	No	61	13	No
13	74	M	Lung	C4	Can	No	No	Yes	45	14	No
14	68	F	Breast	C6, C7	Cannot	No	Lung	No	6	6	No
15	37	M	Unknown	C4	Can	Humerus	No	Yes	35	9	Hematoma
16	69	M	Lung	C2, C3	Can	Rib	No	No	17	10	No
17	69	F	Thyroid	C2	Can	Sternum	Brain	No	7	15	No
18	58	M	Kidney	C7, T1	Cannot	Femur	Bladder	No	5	7	CSF leakage
19	59	F	Breast	C7	Can	Pelvic	Lung, liver	Yes	57	14	No

Abbreviations: BM, bone metastasis; CSF, cerebrospinal fluid; F, female; JOAS, Japanese Orthopaedic Association Score; M, male; MSCC, metastatic spinal cord compression.

Table 3 Brief inventory and JOAS at baseline and following surgery

	Baseline	1 day	1 month	3 months	6 months	12 months
	N=19	N=19	N=18	N=16	N=14	N=8
Worst pain (0–10)						
Score	8.6	5.6	4.5	3.8	2.6	2.4
P-value		<0.001	<0.001	<0.001	<0.001	<0.001
Average pain (0–10)						
Score	7.1	3.2	2.7	2.1	1.7	1.8
P-value		<0.001	<0.001	<0.001	<0.001	<0.001
Pain interference (0–10)						
Score	7.8	4.0	3.3	2.9	2.1	2.0
P-value		<0.001	<0.001	<0.001	<0.001	<0.001
JOAS (0–17)						
Score	11.0	12.0	13.0	14.0	15.0	14.0
P-value		0.469	0.010	<0.001	<0.001	<0.001

Abbreviation: JOAS, Japanese Orthopaedic Association Score.

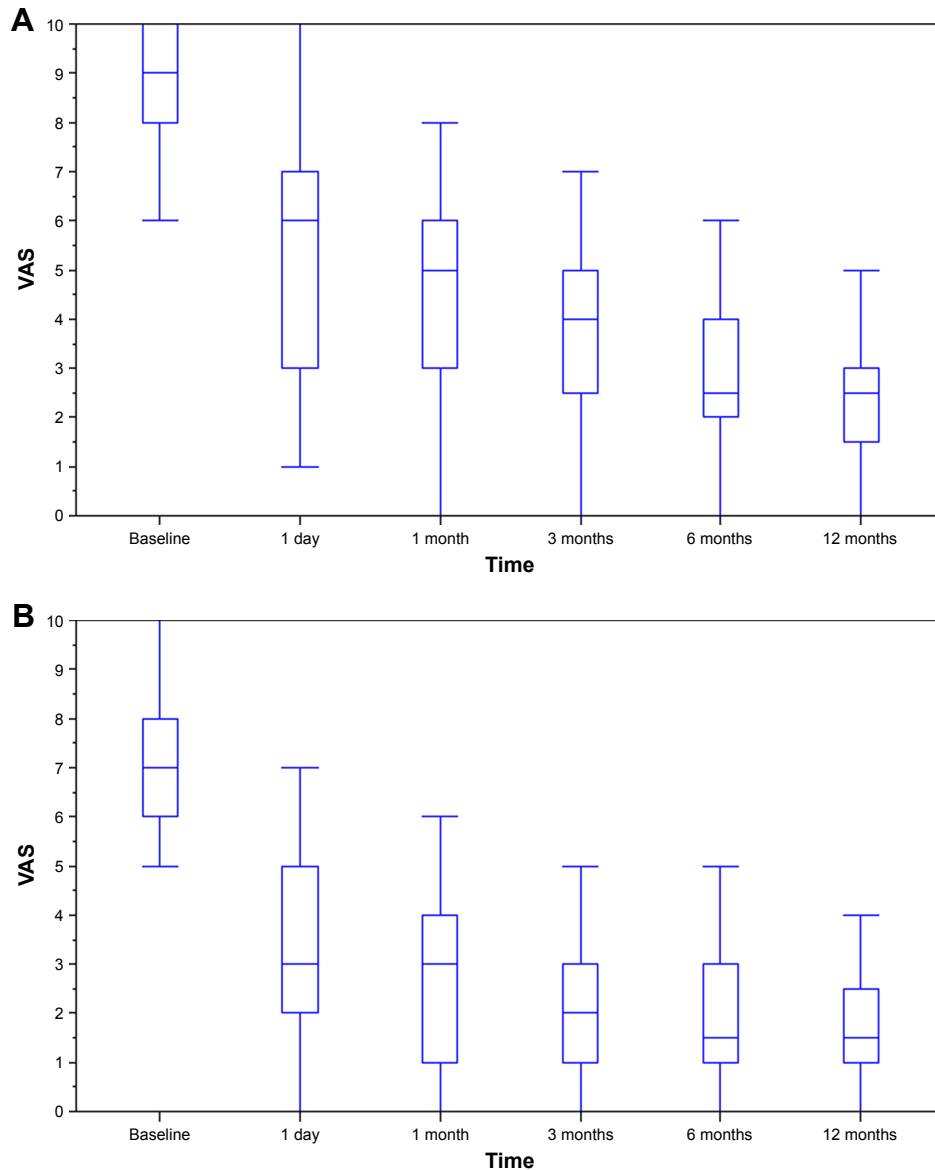


Figure 2 (Continued)

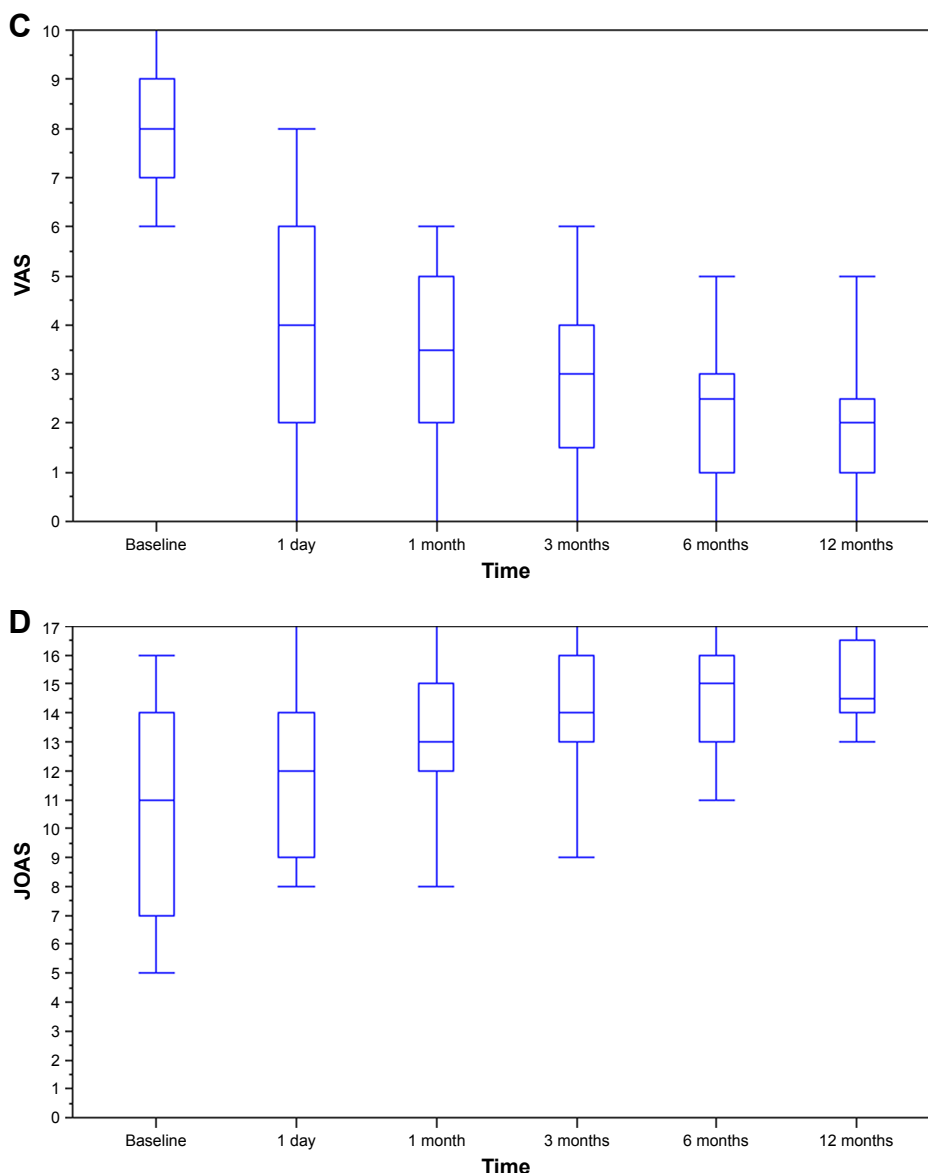


Figure 2 Pain and JOAS at baseline and following surgery: (A) worst pain; (B) average pain; (C) pain interference; (D) JOAS. **Abbreviations:** JOAS, Japanese Orthopaedic Association Score; VAS, visual analog scale.

to longer survival were slow growth cancer, ambulatory ability, ¹²⁵I seed brachytherapy, no surgery-related complication, and higher JOAS (Table 4). Median survival time was 13.7 months (95% CI, 3.0–45.1 months) for patients with slow growth cancer and 6.4 months (95% CI, 1.9–11.5 months) for those with rapid growth cancer, and the difference was significant ($P<0.001$). Besides, patients who were ambulatory had longer median survival time than those who were not (13.7 months; 95% CI, 6.2–31.4 months vs 5.4 months; 95% CI, 0.5–8.2 months) ($P=0.024$). And patients who had undergone ¹²⁵I seed brachytherapy also had longer median survival (20.8 months; 95% CI, 6.4–35.0 months vs 6.2 months; 95% CI, 1.9–13.6 months)

($P=0.034$). Furthermore, patients with postoperative complications (4.1 months; 95% CI, 0.5–11.4 months) were found to have shorter median survival than those without any postoperative complication (13.7 months; 95% CI, 6.4–31.4 months) ($P<0.001$). Finally, compared with patients with lower JOAS (4.4 months; 95% CI, 1.9–11.4 months), patients with higher JOAS were observed to have longer median survival (13.7 months; 95% CI, 6.4–31.4 months) ($P=0.010$). According to the multivariate analysis of survival outcome, the type of primary cancer ($P=0.033$), ambulatory status ($P=0.004$), extra-spinal bone metastasis ($P=0.021$), ¹²⁵I seed brachytherapy ($P=0.014$), and surgery-related complication ($P=0.009$) maintained significance.

Table 4 Prognostic characteristics for survival and neurological outcome

Characteristics	Variables	Survival		Neurological outcome	
		UA	MA	UA	MA
Age	≤57 vs >57 years	0.290	NI	0.876	NI
Sex	Female vs male	0.105	NI	0.410	NI
Type of primary cancer	Slow growth vs rapid growth	<0.001	0.033	0.601	NI
Ambulatory status	Ambulatory vs not ambulatory	0.024	0.004	0.028	NI
Extra-spinal BM	No vs yes	0.108	0.021	0.639	NI
Visceral metastasis	No vs yes	0.489	NI	0.081	NI
Time for developing motor deficit	≤2 vs >2 weeks	0.105	NI	0.081	NI
¹²⁵ I seed brachytherapy	No vs yes	0.034	0.014	0.151	NI
Surgery-related complication	No vs yes	<0.001	0.009	0.019	NI
JOAS	Severe (<10) vs mild (≥10)	0.010	NI	0.013	0.013

Note: Slow growth cancer: breast, thyroid, and renal cancer; rapid growth cancer: lung, esophagus, colorectal cancer, and unknown.

Abbreviations: BM, bone metastasis; JOAS, Japanese Orthopaedic Association Score; MA, multiple analysis; NI, not included; UA, univariate analysis.

JOAS lost significance, while extra-spinal bone metastasis became significant. As for the neurological outcome, ambulatory status ($P=0.028$), surgery-related complication ($P=0.019$), and JOAS ($P=0.013$) had significant impact based on the univariate analysis, while only JOAS ($P=0.013$) showed significance based on the multivariate analysis. Notably, patients with ambulatory ability ($P=0.028$), no surgery-related complication ($P=0.019$), and higher JOAS ($P=0.013$) had better neurological outcome. Besides, patients with no visceral metastasis and shorter time for developing motor deficit also had a better neurological outcome, but both did not reach significance.

Complications

Surgery-related complications occurred in five patients (26.3%). Operation site infection was observed in two cases, which was successfully treated by continuous irrigation. One patient showed epidural hematoma and required surgical removal. Cerebrospinal fluid leakage was found in one case and required percutaneous lumbar drainage. Pneumonia occurred in one case and was controlled by antibiotics.

Discussion

MSCC is an oncological emergency, which initially and reversibly causes edema, venous congestion, and demyelination, and prolonged compression can lead to vascular injury, cord necrosis, and permanent damage. Importantly, patients who have no neurological function for >48 hours are unlikely to improve.¹⁰ Current data suggest that radiation therapy, corticosteroids, and surgery, alone or in combination, can relieve pain and preserve neurologic function.⁷

The commonly used surgical procedures for patients with MSCC include excisional surgery, palliative decompression, and minimally invasive surgery. Excisional surgery can remove the whole metastasis and may realize long-term survival without cancer burden, but its complication rates are very high. Generally speaking, palliative decompression is the standard surgical procedure for MSCC. Palliative decompression, posterior decompression, and spine stabilization, had lesser complication rates, lower bleeding risks, and adequate decompressions as compared with excisional surgery. Thus, rapid decompression and immediate spine stabilization for MSCC has become the standard treatment for MSCC due to its increased efficacy over conventional radiotherapy in preserving neurological function and improving survival prognosis.^{8,11}

Reduction in pain and the preservation of motor function in patients with MSCC may significantly improve the patients' quality of life. Surgery for MSCC in the cervical spine was found to be effective in terms of pain control and neurological recovery. In the present study, the worst pain, average pain, and pain interference showed improvement when preoperative and postoperative pain scores were compared at each time point. In detail, the worst pain relief (a 2-score drop in pain was defined as clinically significant relief) was observed in 78.9% of the patients, average pain relief was achieved in 89.5%, and pain interference relief occurred in 84.2% after surgery. Regarding neurological outcome, postoperative JOAS was increased at each time point as compared with preoperative JOAS. 68.4% of the patients could walk 4 weeks after surgery, 15.8% of the non-ambulatory patients before operation regained the ability to

walk, and 52.6% of the patients maintained their ambulatory status. Similar results were obtained in another prospective multicenter study. Fehlings et al¹² concluded that surgical intervention provided immediate and sustained improvement in pain, neurologic, functional, and patients' quality of life after analyzing 142 MSCC patients. There was an improvement in ambulatory status, lower extremity, and total motor scores at 6 months after surgery. Oswestry Disability Index and pain interference also improved at 6 weeks and 3, 6, and 12 months, postoperatively. Moreover, at 3 months after surgery, the American Spinal Injury Association impairment scale grade improved. Regarding surgical procedure, surgical levels were similar with the cancer-involved levels. Generally, the fusion range was the upper and lower two vertebrae of the surgical levels.

Several prognostic factors have been identified to assess survival prognosis after surgery for spinal metastasis. Tokuhashi et al^{13,14} presented a scoring system including six parameters, ie, general condition, number of extra-spinal bone metastases, number of spinal metastases, the incidence of metastases to a major internal organ, type of primary malignancy, and finally grade of neurological deficit. Sioutos et al¹⁵ found that preoperative neurological status, the anatomic site of the primary carcinoma, and the number of vertebral bodies involved were significantly associated with survival. Robson¹⁰ reported that prognostic indicators that suggest surgery would more likely be beneficial are histological findings such as multiple myeloma, lymphoma, or breast, prostate, or renal cancers, good motor function at presentation, good performance status, limited comorbidity, single-level spinal disease, absence of visceral metastasis, and long interval from primary diagnosis. Bauer and Wedin¹⁶ showed that absence of visceral metastases, solitary skeletal metastases, and type of primary cancer (not lung, breast, and renal cancer, lymphoma or myeloma) were significantly associated with longer survival. Heidecke et al¹⁷ concluded that histology of the primary tumor, the extent of metastasis, and baseline general condition were the most important prognostic factors for survival in patients with cervical metastasis after surgery.

Except for the factors found in the study of Heidecke et al, the above prognostic factors were not specific to cervical spine metastasis after surgery. However, participants in the Heidecke et al study were operated for spine metastasis in general, not particularly for MSCC. In our series, the type of primary cancer, ambulatory status, extra-spinal bone metastasis, ¹²⁵I seed brachytherapy, and surgery-related complication status were found to be significantly associated

with postoperative survival in patients with MSCC in cervical spine after surgery. And, only JOAS had a significant impact on the postoperative neurological outcome. As for the postoperative overall survival and survival rates, the median overall survival was found to be 11.5 months and the 1-year survival rate was 46.3%, which conformed to other studies.^{17,18} Surgery-related complications occurred in 26.3% of the entire cohort of patients and were reported in other studies to occur in 10%–30% of patients.^{12,19,20}

The limitation of this study includes the following aspects. First, the study was based on retrospective data, which unavoidably result in bias. Second, the statistical analyses included only 19 cases and over 10 years of data were used. The changes in diagnosis, treatment, clinical/medical knowledge, etc may remarkably influence the surgical results and postoperative outcomes. Finally, data on systemic treatment following treatment were not available in most patients, which also could bias survival outcome and surgical results. Therefore, a larger and prospective study is warranted.

In conclusion, posterior decompression and spine stabilization for painful cervical spine metastasis resulting from spinal cord compression was found to be effective for neurological recovery and pain control with a tolerable rate of complications. The type of primary cancer, ambulatory status, extra-spinal bone metastasis, ¹²⁵I seed brachytherapy, and surgery-related complications were found to be significantly associated with postoperative survival, and JOAS has a significant impact on the postoperative neurological outcome. These factors can help select the individual treatment methodology for patients with MSCC in the cervical spine.

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Disclosure

The authors report no conflicts of interest in this work.

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