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ORIGINAL RESEARCH

# Surgical results and clinical risks of postoperative complications in patients with painful malignant spinal cord compression after decompressive surgery

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**Introduction:** This study aims to analyze clinical outcome in patients with painful malignant spinal cord compression due to advanced cancers after the decompressive surgery and identify risk factors for postoperative complications in these patients. Furthermore, we created a scoring model to predict the risk of postoperative complications based on identified significant risk factors.

**Methods:** We retrospectively analyzed survival outcomes, pain outcomes, and postoperative complications of patients with painful malignant spinal cord compression who were surgically treated in our department. Identification of risk factors for postoperative complications was also performed, and significant factors according to the multiple logistic regression models were included in the scoring model.

**Results:** As a result, 105 patients were enrolled. The overall median survival time was 9.1 months (95% CI, 7.1–11.4 months). The mean worst pain score was 8.0 in a 24-hour period before surgery, while it decreased to 6.0, 5.0, 3.5, 3.3, and 3.6 (all $P<0.01$, when compared with baseline date) at 1 week, 1 month, 3, 6, and 12 months after surgery, respectively. Similar decreases were also observed in the average pain and the pain interference. Thirty-one complications occurred within 4 weeks after operation in 26 patients (24.8%, 26/105). Based on multiple logistic regression models, age ($P=0.03$), Karnofsky performance status ($P<0.01$), and Charlson Comorbidity Index ($P=0.04$) were significantly associated with postoperative complications and were included in the scoring model. Three risk groups were created based on the complication rates of each scoring points. The corresponding postoperative complication rates of the three groups were 7.7% in group A (0–3 points), 26.7% in group B (4–6 points), and 60.9% in group C (7–10 points), respectively (OR, 4.32, 95% CI: 2.24–8.31, $P<0.01$).

**Conclusion:** Decompressive surgery for painful malignant spinal cord compression was found to be useful for pain control with a tolerable rate of complications. We created a scoring model to predict the risk of postoperative complications in patients with painful malignant spinal cord compression after surgery. This scoring model may guide doctors to choose the appropriate care strategies to realize better pain management.

**Keywords:** pain outcome, postoperative complication, malignant spinal cord compression, decompressive surgery, survival

## Introduction

Spine metastasis, a severe complication of advanced cancers, occurs in up to 50% of cancer patients.[1] The most common spine metastases are from lung, breast, and prostate cancers.[2] Malignant spinal cord compression is resulted from direct compression of the spinal cord due to spine metastasis. Malignant spinal cord compression can lead to neurologic deficits, independence of life routine, and usually persistent and intractable pain, significantly reducing the patient's quality of remaining life.[1,3] An operation could be performed in the spine to improve the quality of the patient's remaining life when patients suffer from the decline in neurologic status or severe pain or clinical evidence of an unstable spine.[4] Besides, the expected survival time of the patients should be >3 months to benefit more from the decompressive surgery.[5–7]

The postoperative complications, including operation site infection, septicemia or sepsis, respiratory complications, intestinal bleeding, epidural hematoma, and so on, facilitate the occurrence of local diseases, burden patient's financial problem, and even cause failure of surgery or decrease patient's survival time.[8,9] Operation site infection was the most common complication. Studies showed that 12.1%–26.6% of patients developed postoperative complications after open surgery in patients with spine or bone metastasis,[2,9–13] and operation site infection was up to 25%.[2] Importantly, complications worsen the pain outcome. Patients with postoperative complication usually suffer from more serious financial losses and pain disturbances.

Notably, several characteristics have been proposed to facilitate surgeons to identify candidates who had high risks of postoperative complications, realize early preventions or interventions, and individualize treatment strategies in patients with malignant spinal cord compression or bone metastasis.[9–11,14] However, to the best of our knowledge, there are few articles addressing the systemic analysis of pain outcome and developing a scoring model to predict the risk of postoperative complications after open surgery in patients with spine metastasis.

Therefore, in the present study, we aim to analyze survival and pain outcomes in patients with painful malignant spinal cord compression after the decompressive surgery and to identify risk factors for postoperative complications in these patients. Furthermore, we created a scoring model to predict the risk of postoperative complications based on identified significant risk factors.

# Materials and methods

## Patients

We retrospectively analyzed patients with spine metastasis between January 2013 and January 2017. Magnetic resonance imaging, supplied by computed tomography scans, confirmed malignant spinal cord compression which was radiographically defined as an epidural metastatic lesion causing displacement of the spinal cord from its normal position. This disease was a vital source of morbidity in patients with advanced cancer. Asymptomatic malignant spinal cord compression was not included in this study, and moderate to severe neurological pain was observed in all patients. We included patients who were treated with operation with open surgical decompression and stabilization (case report is shown in Figure 1), and the indication for surgery was neurological deficit due to spinal cord compression. The diagnosis of bone metastasis was histologically confirmed. We excluded patients who were too sick to undergo surgery. Besides, patients who were treated with the previous radiotherapy were not included, and patients with minimally invasive surgery alone, such as percutaneous vertebroplasty, were also not included in the study. The data were retrospective in nature and anonymized by the Medical Research Ethics Board in the People's Hospital of Henan Province. The Medical Research Ethics Board in the People's Hospital of Henan Province approved this study, and it required neither patient approval nor informed consent for review of patients' images and medical records.

## Pain analysis

The brief pain inventory is a widely used tool to measure pain severity and pain interferes.[15] The pain severity contains four main items, including the worst pain in last 24 hours, the least pain in last 24 hours, the average pain in last 24 hours, and the pain right now. Pain interferences are assessed by seven items in the past 24 hours (general activity, mood, walking ability, healthy walk, relations with other people, sleep, and enjoyment of life). Each pain inventory is ranged from 0 to 10. Zero indicates no pain or no interference and ten indicates pain as bad as the patient can imagine or pain that completely interferes. We measured the worst pain, the average pain, and the pain interference for each patient at baseline and at 1 week, 1 month, 3 months, 6 months, and 12 months following surgery. Postoperative analgesia was routinely performed within 3 days postoperatively. The pain scores were recorded in the patients' records, and that dates were also collected during follow-up.

## Analysis of risk factors

We retrospectively analyzed ten risk factors for postoperative complications in patients with painful malignant spinal cord compression after decompressive surgery. These prognostic factors included gender (female vs male), age (<60 years old vs ≥60 years old, conformed to previous studies), primary tumor sites (slow growth vs moderate growth vs rapid growth), Karnofsky performance status (KPS, 10–40 vs

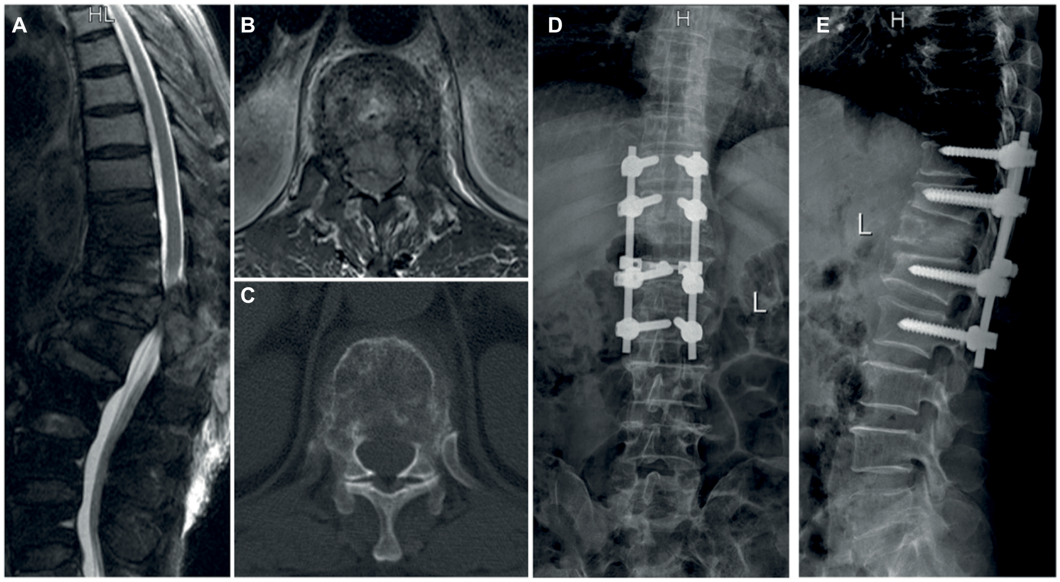


**Figure 1** A 54-year-old woman was diagnosed with lung cancer.
**Notes:** Spinal cord compression occurred in T12 6 months after the diagnosis. She was unable to walk and had serious pain (the average VAS =8) in the back due to malignant spinal cord compression. (**A** and **B**) Preoperative MRI showed pathologic collapse of T12 and serious spinal cord compression. (**C**) Preoperative CT showed bone destruction of T12. (**D** and **E**) Following laminectomy at T12, a pedicle screw fixation was conducted for spine stabilization at T11 and L1. Ambulatory function was recovered, and she was able to walk 1 week after surgery. The average pain score decreased from preoperative 8 to postoperative 2. She was alive at the last follow-up with satisfactory construction of the spine.
**Abbreviations:** CT, computed tomography; MRI, magnetic resonance imaging; VAS, visual analog scale.

50–70 vs 80–100), adjunctive therapies (targets therapy, chemotherapy, or hormone therapy; no vs yes), Charlson Comorbidity Index (CCI) (8 vs ≥9), number of bone metastasis (1–2 vs ≥3), visceral metastases (no vs yes), the time interval from cancer diagnosis to open surgery for spine metastasis (<2 months vs ≥2 months, median time, 2 months), and laboratory examinations (normal vs abnormal). Primary tumors were divided into slow growth cancers, including breast cancer, prostate cancer, and thyroid cancer; moderate growth cancers, including kidney cancer and uterus cancer; and rapid growth cancers, including lung cancer, esophageal carcinoma, liver cancer, stomach cancer, colon cancer, and primary unknown.[5] We used the CCI to estimate the comorbidity before surgery.[16] The score for bone metastasis was 8 points in the CCI, so the patients were classified into those with CCI =8 points and those with CCI ≥9 points. The comorbidities included chronic lung diseases, such as COPD, cardiac disease (coronary heart disease), cerebrovascular disease, hypertension, chronic renal failure, and diabetes. Patients with C-reactive protein ≥0.4 mg/dL, lactic acid dehydrogenase ≥250 IU/L, or serum albumin <3.7 g/dL were regarded as abnormal, which was developed from Katagiri et al.[17] Postoperative complications were recorded intraoperatively or within 4 weeks postoperatively. Postoperative complications were defined as operation site infections, septicemia or sepsis, respiratory complications, cardiac events, intestinal bleeding, epidural hematoma, pulmonary embolism, cerebrovascular events, and acute renal failures.

## Statistical analysis

Analysis of survival was performed using Kaplan–Meier method, and analysis of the visual analog scale (VAS) was performed using repeated measures of the correlated variance model across each time points and Wilcoxon rank sum test. The simple and multiple logistic regression models were used to analyze the preoperative risk factors for postoperative complications. Significant factors for postoperative complications according to the multiple logistic regression models were included in the scoring model. The scoring point for each significant factor was obtained from the odds ratios according to the multiple logistic regression models. The odds ratios were rounded off to the nearest integer. The total prognostic score of each patient represents the sum of all the scores from the significant prognostic characteristics. The patients were divided into several risk groups based on the postoperative complication rate of each score. The simple logistic regression model was used to confirm whether the scoring model was valid. A $P$-value ≤0.05 was considered statistically significant. Statistical analysis was performed using SAS 9.2.

# Results

## Patients' characteristics

As a result, 105 patients were included in the study. In the entire cohort of patients, the median age was 58 years (95% CI: 56–61 years), and 43 patients were aged >60 years old. There were 54 females and 51 males. In this cohort, 24.8% of patients were with slow growth cancers, 12.4% of patients were with moderate growth cancers, and 62.9% of patients were with rapid growth cancers. Lung cancer (47.6%, 50 cases) was the most common primary cancer type, followed by breast cancer (18.1%, 19 cases). In the entire cohort of 105 patients, the overall median survival time was 9.1 months (95% CI, 7.1–11.4 months), and 6-month and 12-month survival rates were 65.4% and 36.8%, respectively. The median length of follow-up was 11.2 months (range: 4.5–18.6 months). At the last follow-up, there were still 11 patients alive with a median survival time of 10.0 months (range: 2.0–26.0 months). The overall survival curve is shown in Figure 2.

## Pain outcome

The mean worst pain score was 8.0 in a 24-hour period before surgery, while it decreased to 6.0, 5.0, 3.5, 3.3, and 3.6 (all $P<0.01$, when compared with baseline, Table 1, and Figure 3A) at 1 week, 1, 3, 6, and 12 months after surgery, respectively. The average pain score was 6.8 in a 24-hour period before surgery, while it decreased to 3.6, 3.6, 3.1, 1.9, and 2.1 (all $P<0.01$, when compared with baseline, Figure 3B) at 1 week, 1, 3, 6, and 12 months after surgery, respectively. Regarding the pain interference score, it was 7.0 in a 24-hour period before surgery and decreased to 5.0, 3.8, 2.8, 3.2, and 2.9 (all $P<0.01$, when compared with baseline, Figure 3C) at 1 week, 1, 3, 6, and 12 months after surgery, respectively. Besides, the worst pain relief (the clinically significant relief), which was defined as a 2-score drop in pain, was obtained in 61.9% of the patients, the average pain relief was observed in 77.1%, and pain interference relief occurred in 62.9% after surgery.

## Complications

Thirty-one complications occurred within 4 weeks of surgery in 24.8% (26/105) of patients. Five patients had double complications. Postoperative complications included operation site infections (eight cases, 7.6%), septicemia or sepsis (four cases, 3.8%), respiratory complications (seven cases, 6.7%), cardiac events (five cases, 4.8%), intestinal bleeding (two cases, 1.9%), epidural hematoma (one case, 1.0%), pulmonary embolism (one case, 1.0%), cerebrovascular events (two cases, 1.9%), and acute renal failure (one case, 1.0%).

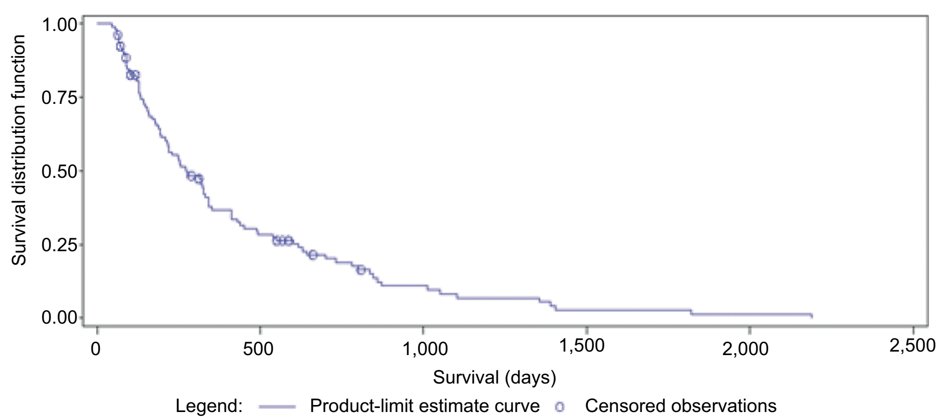


**Figure 2** The overall survival curve (Kaplan–Meier method).

**Table 1** Preoperative and postoperative VAS

| Pain types | Baseline n=105 | 1 week n=105 | 1 month n=104 | 3 months n=80 | 6 months n=65 | 12 months n=34 |
|---|---|---|---|---|---|---|
| Worst pain (0–10) | 8.0 | 6.0[a] | 5.0[a] | 3.5[a] | 3.3[a] | 3.6[a] |
| Average pain (0–10) | 6.8 | 3.6[a] | 3.6[a] | 3.1[a] | 1.9[a] | 2.1[a] |
| Pain interference (0–10) | 7.0 | 5.0[a] | 3.8[a] | 2.8[a] | 3.2[a] | 2.9[a] |

**Note:** [a]$P<0.01$, when compared with baseline.
**Abbreviation:** VAS, visual analog scale.

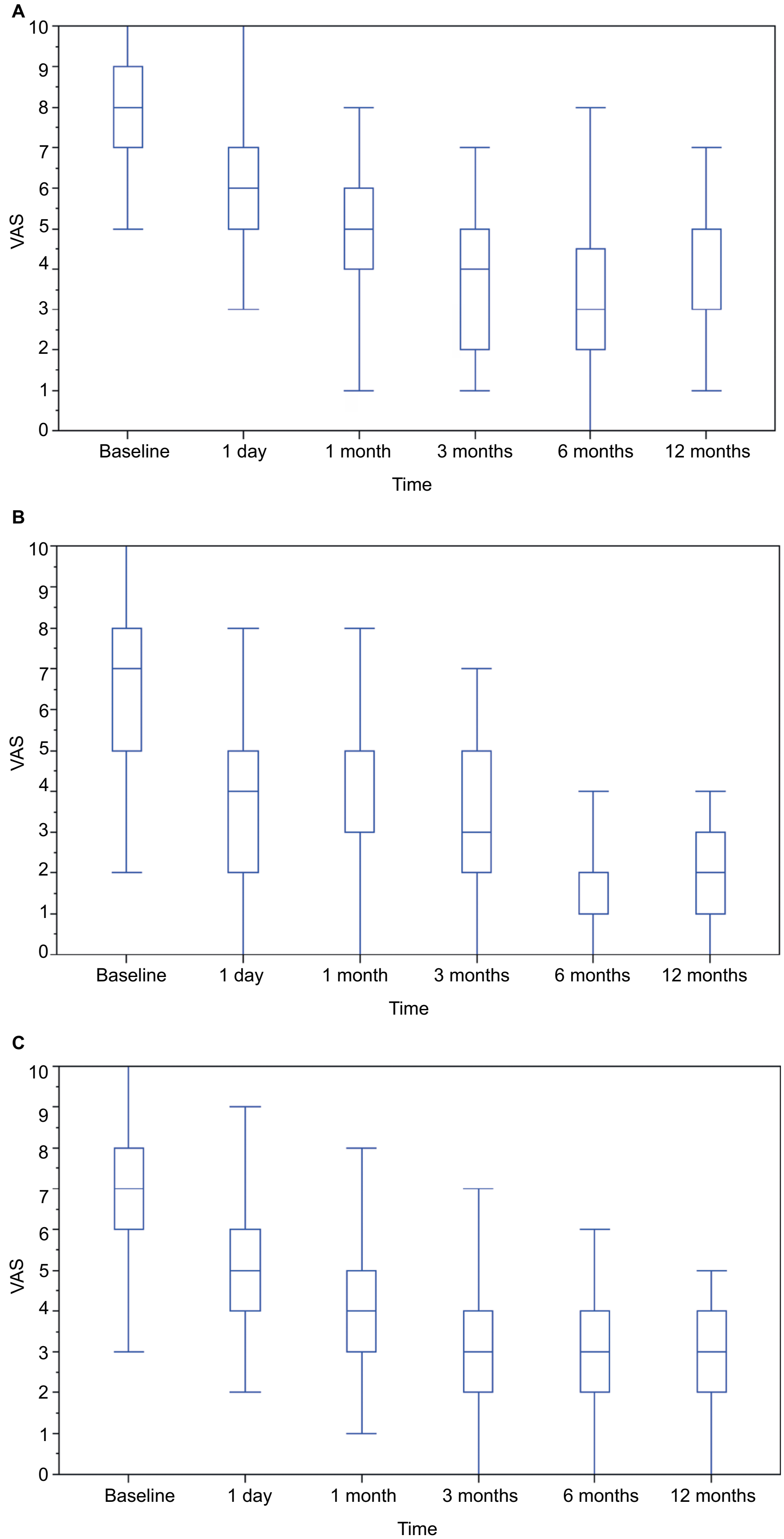


**Figure 3** Preoperative and postoperative pain score (VAS): (**A**) the worst pain, (**B**) the average pain, and (**C**) the pain interference.
**Abbreviation:** VAS, visual analog scale.

## Identification of risk factors

According to the simple logistic regression model, age (OR, 6.22, 95% CI: 2.31–16.74, $P<0.01$), KPS (OR, 4.88, 95% CI: 2.26–10.54, $P<0.01$), adjunctive treatments (OR, 4.10, 95% CI: 1.58–10.62, $P<0.01$), CCI (OR, 3.68, 95% CI: 1.46–9.32, $P<0.01$), and laboratory examinations (OR, 4.33, 95% CI: 1.67–11.25, $P<0.01$) had significant impacts on postoperative complications (Table 2). Based on the multiple logistic regression models, three of the above five prognostic factors were still significantly associated with postoperative complications. Those three significant factors were age (OR, 3.46, 95% CI: 1.15–10.39, $P=0.03$), KPS (OR, 4.24, 95% CI: 1.85–9.70, $P<0.01$), and CCI (OR, 3.17, 95% CI: 1.04–9.62, $P=0.04$; Table 2). Table 3 shows that the scoring points for each of the three significant factors were obtained from the odds ratios (rounded values). The sum of score points from the three significant factors represents the total score of each patient, which resulted in scores of 0, 2, 3, 4, 5, 6, 7, 8, and 10 points. The postoperative complication rate of each score was considered, and the patients were divided into three risk groups: group A (0–3 points, n=52), group B (4–6 points, n=30), and group C (7–10 points, n=23). The corresponding postoperative complication rates were 7.7%, 26.7%, and 60.9%, respectively (OR, 4.32, 95% CI: 2.24–8.31, $P<0.01$). There was a case report. If a 62-year-old patient with moderate KPS had a CCI of 8 points, then total score of the patient was 5 points (3 points +2 points +0 point). Thus, this patient would be classified as group B with a complication rate of about 26.7%.

**Table 2** Univariate and multivariate analyses of preoperative factors for perioperative complications in patients with spine metastasis after open surgery

| Characteristics | Patients (n) | Simple logistic regression | | Multiple logistic regression | |
|---|---|---|---|---|---|
| | | OR (95% CI) | *P*-value | OR (95% CI) | *P*-value |
| **Gender** | | | | | |
| Female | 54 | 0.90 (0.36–2.14) | 0.78 | NI | |
| Male | 51 | | | | |
| **Age** | | | | | |
| <60 years | 62 | 6.22 (2.31–16.74) | <0.01 | 3.46 (1.15–10.39) | 0.03 |
| ≥60 years | 43 | | | | |
| **Primary tumor sites** | | | | | |
| Slow growth | 26 | 1.30 (0.79–2.15) | 0.30 | NI | |
| Moderate growth | 13 | | | | |
| Rapid growth | 66 | | | | |
| **KPS** | | | | | |
| Poor | 22 | 4.88 (2.26–10.54) | <0.01 | 4.24 (1.85–9.70) | <0.01 |
| Moderate | 48 | | | | |
| Good | 35 | | | | |
| **Adjunctive treatments** | | | | | |
| Yes | 59 | 4.10 (1.58–10.62) | <0.01 | NI | |
| No | 46 | | | | |
| **CCI** | | | | | |
| 8 | 72 | 3.68 (1.46–9.32) | <0.01 | 3.17 (1.04–9.62) | 0.04 |
| ≥9 | 33 | | | | |
| **Number of bone metastasis** | | | | | |
| 0–2 | 30 | 1.12 (0.41–3.01) | 0.83 | NI | |
| ≥3 | 75 | | | | |
| **Visceral metastases** | | | | | |
| Yes | 46 | 1.39 (0.57–3.39) | 0.46 | NI | |
| No | 59 | | | | |
| **Time interval from cancer diagnosis to open surgery** | | | | | |
| <2 months | 53 | 2.26 (0.90–5.67) | 0.08 | NI | |
| ≥2 months | 52 | | | | |
| **Laboratory examinations** | | | | | |
| Normal | 60 | 4.33 (1.67–11.25) | <0.01 | NI | |
| Abnormal | 45 | | | | |

**Abbreviations:** CCI, Charlson Comorbidity Index; KPS, Karnofsky performance status; NI, not included; OR, odds ratio.

**Table 3** A scoring model for predicting the risk of perioperative complications in patients with spine metastasis after open surgery

| Prognostic factors | OR | Scores |
|---|---|---|
| **Age** | | |
| <60 years | 3.46 | 0 |
| ≥60 years | | 3 |
| **KPS** | | |
| Poor | 4.24 | 4 |
| Moderate | | 2 |
| Good | | 0 |
| **CCI** | | |
| 8 | 3.17 | 0 |
| ≥9 | | 3 |
| **Prognostic groups** | Patients (n) | |
| Group A | 0–3 | 52 |
| Group B | 4–6 | 30 |
| Group C | 7–10 | 23 |

**Abbreviations:** CCI, Charlson Comorbidity Index; KPS, Karnofsky performance status; OR, odds ratio.

## Discussion

Spinal cord compression resulted from metastatic cancers can lead to neurologic deficits, independence of life routine, and usually persistent and intractable pain, significantly reducing the patient's quality of remaining life.[1,3] Nearly 90% of patients with this disease suffer from severe pain. Besides, postoperative complications after surgery for spine metastasis hold remarkable challenges for surgeons because they may exacerbate or trigger surgical morbidities, worsen pain, and even further aggravate the existing functional deficits.[18] Notably, researchers have shown that 12.1%–26.6% of patients with spine metastasis or bone metastasis developed postoperative complications after open surgery,[2,9–13] which led to the significantly impaired quality of remaining life. 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, which suggested that decompressive surgery for painful malignant spinal cord compression was found to be effective regarding pain controls. In details, the worst pain relief (the clinically significant relief), which was defined as a 2-score drop in pain, was obtained in 61.9% of the patients, the average pain relief was observed in 77.1%, and pain interference relief occurred in 62.9% after surgery. The overall median survival time was 9.1 months in the entire cohort of patients. A similar overall median survival time was observed in other studies.[7,19]

In this study, 31 complications occurred within 4 weeks of surgery in 24.8% (26/105) of patients. A better understanding of the characteristics associated with postoperative complications could provide essential information to identify candidates with high risks of complications, thus realizing early preventions or interventions, facilitating individualization of treatment strategies, and leading to better pain outcome and satisfaction in spine metastasis patients after open surgical decompression and stabilization.[18]

Fortunately, several studies have been proposed to identify factors for postoperative complications. Tsuda et al[10] retrospectively analyzed 1,497 patients with pathological femur fracture resulted from bone metastasis who underwent internal fixation or endoprosthetic reconstruction of the proximal femur. Multivariable logistic regression analysis showed that older age, type of primary tumor, higher CCI, and blood transfusion were significantly associated with postoperative complications. Ju et al[11] reviewed 27 patients with prostate cancer who underwent spinal surgery for metastatic spinal cord compression. They reported that 23% of patients experienced complications, and younger age and instrumentation greater than seven spinal levels were associated with increased risk of complications. In a retrospective and case–control study, Omeis et al[18] concluded that previous spinal surgeries, complex plastic closures, increasing number of comorbidities, presence of a hospital-acquired infection at the time of a previous surgery, and increasing duration of hospital stay during primary surgery were significantly associated with increased likelihood of developing postoperative surgical site infections after reviewing 678 patients with non-sacral tumors. Two hundred patients with metastatic tumors were included in this study and 9.5% of those patients (ie patients with metastatic tumors) developed surgical site infections. Whether preoperative radiotherapy had a significant impact on postoperative complications is still under debate. Itshayek et al[20] found that surgery within 7 days of radiotherapy may increase the likelihood of postoperative wound complications, while Nemelc et al[21] concluded that preoperative radiotherapy had no influence on the postoperative incidence of deep surgical wound infections. Thus, patients with previous radiotherapy were not included in the study to avoid hidden bias.

To the best of our knowledge, there are very few articles developing a scoring model for prediction of postoperative complications in patients with spine metastasis after surgery. In the current study, we found that age, KPS, and CCI were significantly associated with postoperative complications by the multiple logistic regression models after analyzing 105 surgically treated patients with spine metastasis. These findings were consistent with previous studies.[2,9–11,18] Furthermore, we created a scoring model to predict the postoperative complication risks based on the above significant characteristics. The scoring point for each significant characteristic was obtained from the odds ratios according to the multiple logistic regression models. As a result, patients <60 years were regarded as having 0 point and patients ≥60 years as 3 points; patients with poor KPS were regarded as having 4 points, moderate status as 2 points, and good status as 0 point; and patients with CCI =8 were regarded as having 0 point and ≥9 as 3 points. The total prognostic score of each patient represents the sum of all the scores from the significant prognostic characteristics. Furthermore, the patients were divided into three risk groups based on the postoperative complication rate of each score. The corresponding postoperative complication rates were 7.7% in group A (0–3 points), 26.7% in group B (4–6 points), and 60.9% in group C (7–10 points), respectively ($P$<0.01).

## Limitations

This study has some limitations. First, this was a retrospective study; a hidden bias has occurred during patient selection and its possibility could not be avoided. Second, some data, such as blood loss, were not available in all patients, so we could not systematically analyze some patients' characteristics. Third, asymptomatic malignant spinal cord compression was excluded, and thus this scoring system is not suitable for those patients. Lastly, the study did not have controls. Thus, a prospective study proposing to validate the scoring model is truly warranted.

## Conclusion

Decompressive surgery for painful malignant spinal cord compression was found to be useful for pain control with a tolerable rate of complications. We found that patients with age >60 years, poor KPS, and CCI ≥9 points were significantly associated with increased likelihood of postoperative complications. A scoring model was created based on the above three significant characteristics to predict the risk of postoperative complications in patients with malignant spinal cord compression after decompressive surgery. Patients with scores of 7–10 points have the highest risk of suffering from postoperative complications; so, the management of comorbidities before surgery, careful pain management after surgery, and any attempt to control preoperative risk factors should be performed to improve patient's overall clinical outcomes. Still, a prospective study is needed.

## Acknowledgments

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## Disclosure

The authors report no conflicts of interest in this work.

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