# Effect of radiotherapy on local control and overall survival in spinal metastasis of non-small-cell lung cancer after surgery and systemic therapy

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## Aims

Radiotherapy is a well-known local treatment for spinal metastases. However, in the presence of postoperative systemic therapy, the efficacy of radiotherapy on local control (LC) and overall survival (OS) in patients with spinal metastases remains unknown. This study aimed to evaluate the clinical outcomes of post-surgical radiotherapy for spinal metastatic non-small-cell lung cancer (NSCLC) patients, and to identify factors correlated with LC and OS.

## Methods

A retrospective, single-centre review was conducted of patients with spinal metastases from NSCLC who underwent surgery followed by systemic therapy at our institution from January 2018 to September 2022. Kaplan-Meier analysis and log-rank tests were used to compare the LC and OS between groups. Associated factors for LC and OS were assessed using Cox proportional hazards regression analysis.

## Results

Overall, 123 patients with 127 spinal metastases from NSCLC who underwent decompression surgery followed by postoperative systemic therapy were included. A total of 43 lesions were treated with stereotactic body radiotherapy (SBRT) after surgery and 84 lesions were not. Survival rate at one, two, and three years was 83.4%, 58.9%, and 48.2%, respectively, and LC rate was 87.8%, 78.8%, and 78.8%, respectively. Histological type was the only significant associated factor for both LC ($p = 0.007$) and OS ($p < 0.001$). Treatment with targeted therapy was significantly associated with longer survival ($p = 0.039$). The risk factors associated with worse survival were abnormal laboratory data ($p = 0.021$), lesions located in the thoracic spine ($p = 0.047$), and lumbar spine ($p = 0.044$). This study also revealed that postoperative radiotherapy had little effect in improving OS or LC.

## Conclusion

Tumour histological type was significantly associated with the prognosis in spinal NSCLC metastasis patients. In the presence of post-surgical systemic therapy, radiotherapy appeared to be less effective in improving LC, OS, or quality of life in spinal NSCLC metastasis patients.

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## Take home message

- This study demonstrates the necessity of radiotherapy for spinal metastatic non-small-cell lung cancer (NSCLC) patients in the presence of post-surgical systemic therapy.

- This study help to determine the therapeutic therapy for spinal metastatic NSCLC patients.

## Introduction

Lung cancer represents the most frequently diagnosed cancer and the leading cause of cancer-related deaths in the world.[1] Non-small-cell lung cancer (NSCLC) is the most common type of lung cancer and accounts for more than 80% of all cases.[2] Approximately 70% of the patients with late-stage NSCLC develop bone metastasis, where the spinal column is the most common site involved.[3] Spinal metastasis of NSCLC frequently results in bone destruction, pathological fracture, severe bone pain, and neurological deficits. Remarkable progress in systemic therapies, such as chemotherapy, targeted therapy, and immunotherapy, has prolonged life expectancy for patients with NSCLC.[4] Thus, both local control (LC) and quality of life (QoL) will be considered in the decision-making for NSCLC spinal metastasis. A multidisciplinary approach consisting of radiotherapy, surgical treatment, and systemic therapy is emphasized for treating metastatic spinal cancers.[5,6]

Radiotherapy is a well-known local treatment for bone metastasis, and timely postoperative radiotherapy was reported to improve clinical outcomes.[7] Several studies have demonstrated that intensity-modulated radiotherapy (IMRT) or stereotactic body radiotherapy (SBRT) can provide long-term local control and pain relief.[8-10] Radiotherapy was also reported to exert an improved effect when combined with systemic therapy.[11,12] In our institution (the Second Affiliated Hospital of Zhejiang University School of Medicine, China), all patients with spinal metastatic NSCLC are advised to receive chemotherapy or/and targeted therapy as the first-line systemic therapy, as well as radiotherapy for LC after surgery. But in real life, many patients do not receive timely radiotherapy for a variety of reasons. In a developing country like China, where radiotherapists and equipment are scarce, it is a great challenge to meet the needs of a large patient population for timely radiotherapy. Besides, many patients refuse to receive postoperative radiotherapy for several reasons, including poor condition after spine surgery, conceptual conflict (e.g. traditional belief that some patients refuse to receive radiotherapy), and cost concerns.

In our follow-up, many patients were not commonly treated with radiotherapy. Surprisingly, no significant improvement seemed to be observed in oncological outcomes for the use of radiotherapy in spinal metastasis for NSCLC. Furthermore, few studies have verified the necessity of radiotherapy after surgical treatment for spinal metastases in the presence of postoperative systemic therapy. Therefore, we performed this study to demonstrate the necessity of radiotherapy for spinal metastatic NSCLC patients, which will contribute to determining the therapeutic strategy.

## Methods

### Study design and patients

This retrospective study was approved by the Human Research Ethics Committee of the Second Affiliated Hospital of Zhejiang University School of Medicine, China. We retrospectively reviewed the files of patients who underwent decompression surgery for spinal metastases from NSCLC at our centre from January 2018 to September 2022 (Figure 1). The exclusion criteria were as follows: 1) incomplete follow-up data; 2) previous surgery at the treatment site; 3) follow-up period < three months; 4) no postoperative chemotherapy; and 5) received radiotherapy but the time interval between surgical treatment and postoperative radiotherapy was longer than six months. Patients were divided into the "radiotherapy" group or "non radiotherapy" group according to whether they received postoperative SBRT. SBRT was performed at Hangzhou Cancer Hospital, China. All lesions of spinal metastasis were required to be analyzed for targeted molecules, and patients were recommended to receive targeted therapy if available.

### Data collection

Patient, tumour, and treatment characteristics were collected from electronic medical records, including sex, age, follow-up time, tumour histology, location, BMI, vertebral body fracture, laboratory data, tumour size, epidural spinal cord compression (ESCC) grade,[13] Spinal Instability Neoplastic Score (SINS),[14] revised Tokuhashi score,[15] systemic therapy method, radiotherapy method, overall survival (OS), and LC. Each patient was assessed for survival and LC from the day of surgery. Patients underwent CT, MRI, and PET before surgery. Patients after surgery were required to have CT or/and MRI examinations every one to three months for the first year, and every six months thereafter during the follow-up to identify any local progression (Figure 2). Imaging data were reviewed by two experienced observers (a radiologist (HD) and an orthopaedic surgeon (NL)). Laboratory data were reported as a potential prognostic factor,[16] and classified into two groups (normal vs abnormal) according to the standard of our centre. Platelet count (< $1.0\times10^5$ / μl), serum albumin (< 3.5 g/dl), total bilirubin (≥ 21 μmol/l), lactate dehydrogenase (LDH) (≥ 248 IU/l), CRP (≥ 1.0 mg/dl), or serum calcium level (≥ 10.3 mg/dl) were all considered abnormal laboratory data. In this study, 55 patients had normal laboratory results before surgery, while 72 patients had abnormal laboratory results.

The primary endpoint of this study was the LC of the surgical site due to spinal metastases and the secondary endpoint was OS. Local progression was determined according to recommendations by the SPIne response assessment in Neuro Oncology (SPINO).[17] OS was measured until the time of death or last follow-up. QoL was evaluated using the numerical Rating Scale (NRS) score,[18] Karnofsky performance status (KPS) score,[19] mobility (bedridden, wheelchair, double-crutches, single-crutches, or walking independently were assigned 0 to 4 points via an internal score, respectively), and sphincter dysfunction (0 for negative or 1 for positive (intenal score)).

### Statistical analysis

Descriptive statistics were used to describe the characteristics of all the patients. Independent-samples *t*-test was conducted for continuous variables with normal distribution. For variables with skewed distribution, Mann-Whitney U test was used. The chi-squared test was conducted for categorical variables. Univariate and multivariate Cox proportional hazards regression analyses were used to investigate the independent risk factors for LC and OS in patients with NSCLC. Stepwise selection was conducted to determine the final regression

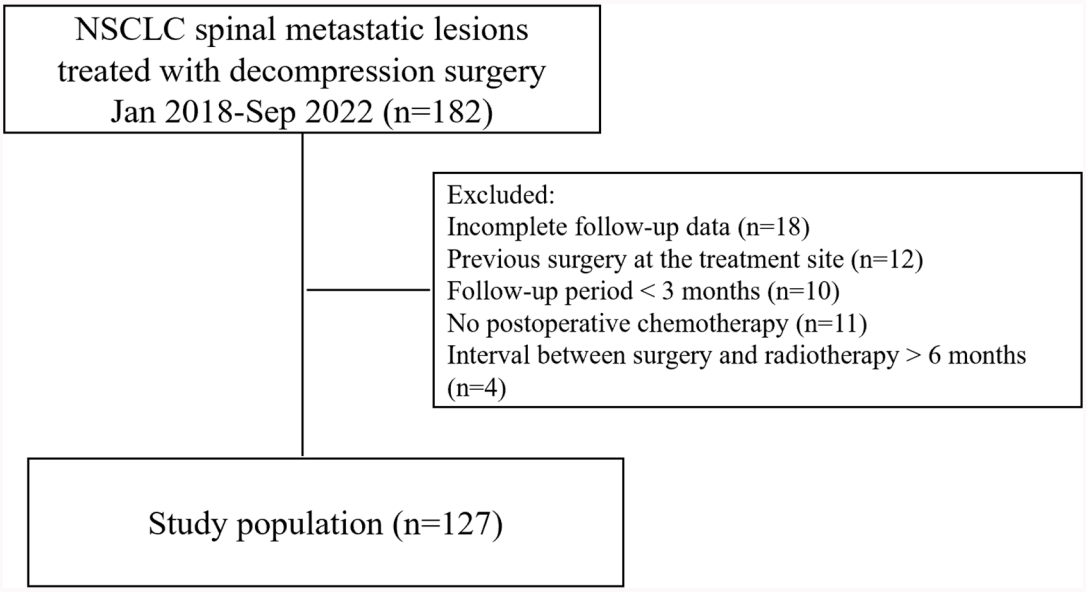


**Fig. 1**
Study chart. NSCLC, non-small-cell lung cancer.

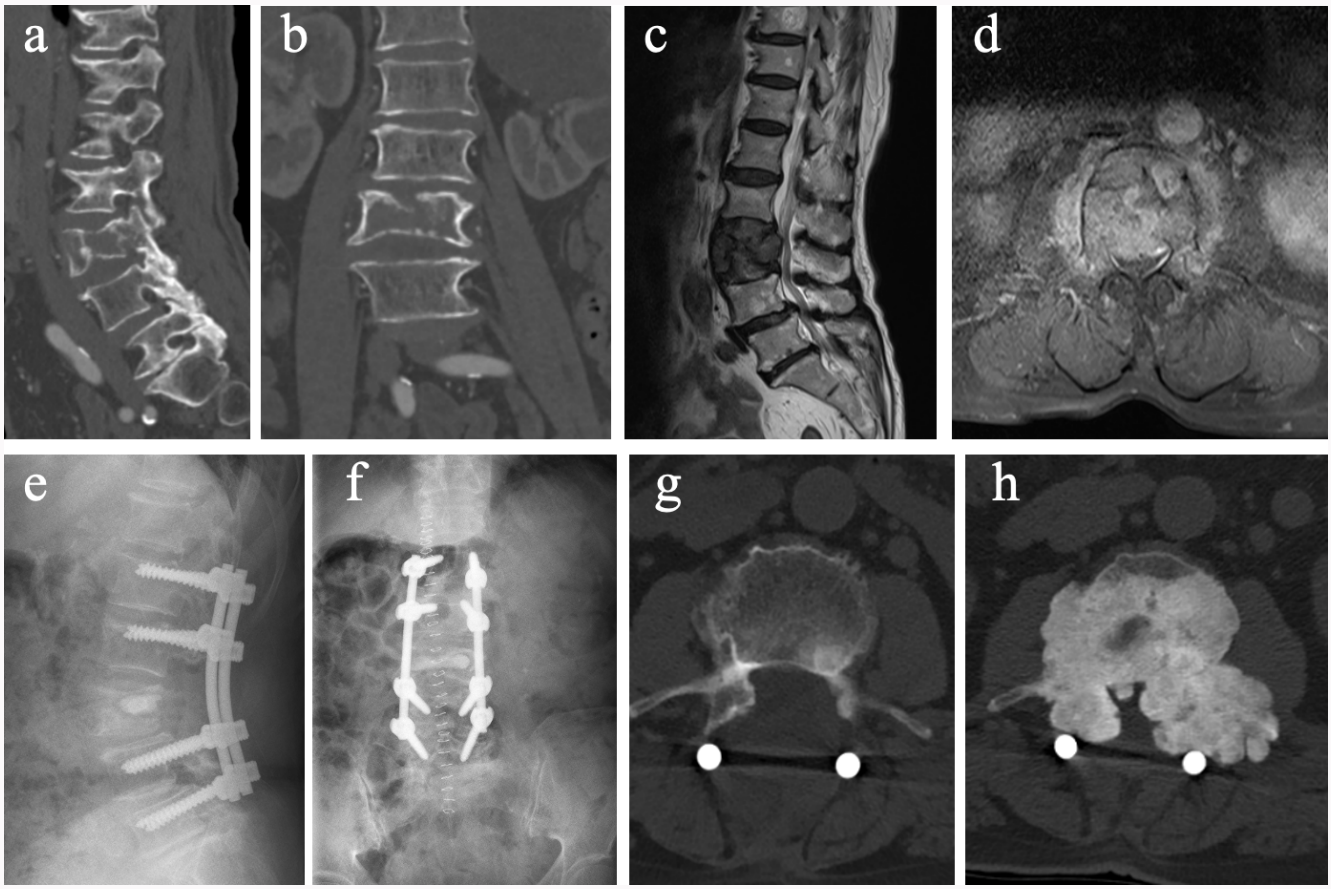


**Fig. 2**
Representative imaging of local progression after surgery in a spinal non-small-cell lung cancer (NSCLC) patient during the follow-up period. A 68-year-old female with L3 metastatic NSCLC experienced severe back pain and weakness for nearly one month. a) and b) Preoperative sagittal and axial CT imaging showed that the lesion was located at L3, accompanied by significant bone destruction. c) and d) Sagittal and axial T2-weighted magnetic resonance imaging before surgery showed that a lesion located in L3 with high-grade epidural spinal cord compression (ESCC). e) and f) Decompression surgery was performed and postoperative radiograph showed good fixation. g) and h) Postoperative axial CT scanning showed that compared with the image five days after operation. h) Significant local progression was observed in the image one year after operation.

model. Both the survival and tumour control rate were calculated, and the impact of postoperative radiation therapy was evaluated using the Kaplan-Meier analysis. The log-rank test was used to assess statistical equivalence between groups. Statistical significance was set at $p < 0.05$. All the above statistics were conducted using R studio v. 1.3.1073 (R Foundation for Statistical Computing, Austria).

## Results

### Patient and tumour characteristics

We identified 123 patients with 127 spinal metastases from lung cancer who underwent decompression surgery followed by postoperative systemic therapy at our institution from January 2018 to September 2022 (Table I). The median follow-up time after surgery was 20 months (interquartile range 10 to 28). The mean age at the time of surgery was 61.6 years (33 to 84). The most common histological type was adenocarcinoma (101/127; 79.6%), followed by squamous cell carcinoma (13/127; 10.2%) and others (13/127; 10.2%). Of these lesions, 43 (33.9%) were treated with SBRT, mostly within six weeks after the surgery when the wound healed and the general condition improved, and they were assigned to the "radiotherapy" group. The remaining 84 lesions that did not receive post-surgical SBRT were assigned to the "non-radiotherapy" group. Various dose schedules were used, with 30 Gy in ten fractions being the most commonly chosen, ranging from 15 to 40 Gy in five to 25 fractions. After surgical treatment, 31 lesions (24.4%) received chemotherapy only and 96 lesions (75.6%) were treated with chemotherapy plus targeted therapy, including epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKI) and anaplastic lymphoma kinase (ALK) inhibitors.

### Clinical outcomes

According to Kaplan-Meier analysis, the one-, two-, and three-year LC rates were 87.8%, 78.8%, and 78.8%, respectively (Figure 3a). LC was maintained in 101 lesions (79.5%), while 26 lesions (20.5%) showed local progression during the follow-up period. The LC rate of patients in the radiotherapy group and the non-radiotherapy group was 87.5% and 87.8%, respectively, at one year, and 76.7% and 80.4%, respectively, at three years (Figure 3b). Univariate and multivariate analysis were performed to assess the risk factors associated with LC (Table II). In univariate analysis, SINS score > 12 (hazard ratio (HR) 2.375; 95% confidence interval (CI) 1.029 to 5.485; $p = 0.043$), squamous cell carcinoma (HR, 2.925; 95% CI 1.072 to 7.979; $p = 0.036$), and other histological types (HR 3.097; 95% CI 1.026 to 9.347; $p = 0.045$) were adversely associated with LC. Although not statistically significant, there were some other strongly associated factors for LC, including revised Tokuhashi score > 8 (HR 0.372; 95% CI 0.128 to 1.083; $p = 0.070$), and lesions located in the thoracic spine (HR 2.882; 95% CI 0.828 to 10.04; $p = 0.096$) and lumbar spine (HR 2.899; 95% CI 0.784 to 10.71; $p = 0.111$). In multivariate analysis, squamous cell carcinoma (HR 4.571; 95% CI 1.501 to 13.92; $p = 0.007$), and lesions located in the thoracic spine (HR 3.714; 95% CI 1.016 to 13.58; $p = 0.047$) and lumbar spine (HR 3.958; 95% CI 1.036 to 15.12; $p = 0.044$) were found to be independent risk factors for LC. Other histological type (HR 3.488; 95% CI 0.945 to 12.87; $p = 0.061$) and revised Tokuhashi score > 8 (HR 0.364; 95% CI 0.124 to 1.072; $p = 0.067$) tended to be significantly associated with LC. Surprisingly, the LC rate was not significantly different between patients who received radiotherapy and those who did not, indicating radiotherapy was not effective for controlling spinal recurrence in the presence of systemic therapy.

For the entire cohort, the one-, two-, and three-year OS rates were 83.4%, 58.9%, and 48.2%, respectively (Figure 4a). A total of 47 patients died during the follow-up. The OS rate of patients in the radiotherapy group and non-radiotherapy group was 77.9% and 86.4%, respectively, at one year, and 55.4% and 43.4%, respectively, at three years (Figure 4b). As shown in Table III, in univariate analysis via multivariate Cox proportional hazards regression, six prognostic factors were found to be adversely associated with OS, which are male sex (HR 1.914; 95% CI 1.052 to 3.480; $p = 0.033$), abnormal laboratory data before surgery (HR 2.132; 95% CI 1.158 to 3.925; $p = 0.015$), SINS > 12 (HR 2.037; 95% CI 1.047 to 3.960; $p = 0.036$), post-surgical chemotherapy plus targeted therapy (HR 0.392; 95% CI 0.207 to 0.743; $p = 0.004$), squamous cell carcinoma (HR 5.033; 95% CI 2.530 to 10.01; $p < 0.001$), and other histological types (HR 3.344; 95% CI 1.359 to 8.224; $p = 0.009$). In multivariate analysis via multivariate Cox proportional hazards regression, abnormal laboratory data before surgery (HR 2.104; 95% CI 1.121 to 3.948; $p = 0.021$), post-surgical chemotherapy plus targeted therapy (HR 0.450; 95% CI 0.211 to 0.960; $p = 0.039$), and squamous cell carcinoma (HR 6.018; 95% CI 2.823 to 12.83; $p < 0.001$) were demonstrated to be three independent prognostic factors for OS. Compared with adenocarcinoma, other histological types (HR 2.503; 95% CI 0.863 to 7.261; $p = 0.091$) and SINS > 12 (HR 1.847; 95% CI 0.926 to 3.684; $p = 0.081$) were correlated with worse OS without statistically significant differences. No significant association was found between OS and postoperative radiotherapy according to this analysis.

We further analyzed the differences in function outcomes between the patients treated with and without postoperative radiotherapy (Table IV). The mean NRS, KPS, and mobility scores for all patients at the last follow-up were 2.59 (standard deviation (SD) 2.84), 63.7 (SD 17.3), and 4.00 (SD 1.77), respectively. No significant improvement was shown among patients treated with radiotherapy. All these results in this study revealed that radiotherapy is less necessary for spinal NSCLC metastasis patients after surgery in the presence of post-surgical systemic therapy.

## Discussion

The majority of NSCLC patients develop spinal metastases, and unsatisfactory prognosis is usually expected in those patients.[20] As long as surgery is an option, surgical treatment combined with radiotherapy is considered the mainstay treatment of choice.[21] Previous literature has demonstrated that SBRT was correlated with a better LC in spinal metastases.[22,23] Radiotherapy was also reported to improve tumour control when combined with separation surgery.[24] Conventional radiotherapy was found to be less effective in tumour control when compared to surgery combined with radiotherapy, emphasizing the importance of surgical resection in treating spinal metastatic cancer.[25] Interestingly, few studies have demonstrated whether surgery combined with postoperative radiotherapy provides better LC than standalone surgery in treating spinal metastases, especially in the presence of

**Table I.** Patient and tumour characteristics.

| Variable | Total | Non-radiotherapy | Radiotherapy | p-value |
|---|---|---|---|---|
| **Sex, n (%)** | | | | 0.190* |
| Female | 62 (48.8) | 45 53.6) | 17 (39.5) | |
| Male | 65 (51.2) | 39 (46.4) | 26 (60.5) | |
| Mean age, yrs (range) | 61.6 (33 to 84) | 61.9 (33 to 84) | 61.0 (36 to 77) | 0.872† |
| Mean follow-up time, mths (range) | 20.7 (3 to 56) | 19.3 (3 to 56) | 24.0 (7 to 48) | 0.091‡ |
| **Histological type, n (%)** | | | | 0.403§ |
| Adenocarcinoma | 101 (79.6) | 65 (77.4) | 36 (83.7) | |
| Squamous cell carcinoma | 13 (10.2) | 11 (13.1) | 2 (4.7) | |
| Others | 13 (10.2) | 8 (9.5) | 5 (11.6) | |
| **Location, n (%)** | | | | 0.974§ |
| Cervical | 32 (25.2) | 21 (25.0) | 11 (25.6) | |
| Thoracic | 56 (44.1) | 38 (45.2) | 18 (41.8) | |
| Lumbar | 36 (28.3) | 23 (27.4) | 13 (30.2) | |
| Sacrum | 3 (2.4) | 2 (2.4) | 1 (2.3) | |
| **BMI, kg/m$^2$, n (%)** | | | | 0.738§ |
| < 18.5 | 8 (6.3) | 6 (7.1) | 2 (4.7) | |
| 18.5 to 23.9 | 83 (65.4) | 56 (66.7) | 27 (62.8) | |
| > 23.9 | 36 (28.3) | 22 (26.2) | 14 (32.5) | |
| **Vertebral body fracture, n (%)** | | | | 0.794§ |
| None | 50 (39.4) | 31 (36.9) | 19 (44.2) | |
| < 50% collapse | 64 (50.4) | 44 (52.4) | 20 (46.5) | |
| > 50% collapse | 13 (10.2) | 9 (10.7) | 4 (9.3) | |
| **Laboratory data, n (%)** | | | | 0.142* |
| Normal | 55 (43.3) | 32 (38.1) | 23 (53.5) | |
| Abnormal | 72 (56.7) | 52 (61.9) | 20 (46.5) | |
| **Tumour size, n (%)** | | | | 0.331* |
| ≤ 50% body involved | 53 (41.7) | 32 (38.1) | 21 (48.8) | |
| > 50% body involved | 74 (58.3) | 52 (61.9) | 22 (51.2) | |
| **ESCC grade, n (%)** | | | | 0.561§ |
| < 2 | 9 (7.1) | 5 (6.0) | 4 (9.3) | |
| ≥ 2 | 118 (92.9) | 79 (94.0) | 39 (90.7) | |
| **SINS, n (%)** | | | | 0.649* |
| 0 to 12 | 102 (80.3) | 66 (78.6) | 36 (83.7) | |
| 13 to 18 | 25 (19.7) | 18 (21.4) | 7 (16.3) | |
| **Revised Tokuhashi score, n (%)** | | | | 0.571 |
| 0 to 8 | 94 (74.0) | 64 (76.2) | 30 (69.8) | |
| 9 to 15 | 33 (26.0) | 20 (23.8) | 13 (30.2) | |
| **Post-surgical systemic therapy, n (%)** | | | | 0.382* |
| Chemotherapy | 31 (24.4) | 18 (21.4) | 13 (30.2) | |
| Chemotherapy + targeted therapy | 96 (75.6) | 66 (78.6) | 30 (69.8) | |

*Chi-squared test.
†Independent-samples *t*-test.
‡Mann-Whitney U test.
§Fisher's exact test.
ESCC, epidural spinal cord compression; SINS, Spine Instability Neoplastic Score.

**Table II.** Results of univariate and multivariate Cox regression analyses of local control rate.

| | | | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|---|---|
| **Variable** | **Regions, n** | **Events, n** | **HR** | **95% CI** | **p-value** | **HR** | **95% CI** | **p-value** |
| **Sex** | | | | | | | | |
| Female | 62 | 13 | Reference | | | Reference | | |
| Male | 65 | 13 | 1.049 | 0.485 to 2.267 | 0.903 | 0.511 | 0.207 to 1.261 | 0.145 |
| **Age, yrs** | | | | | | | | |
| < 65 | 80 | 14 | Reference | | | | | |
| ≥ 65 | 47 | 12 | 1.535 | 0.709 to 3.323 | 0.276 | | | |
| **Location** | | | | | | | | |
| Cervical spine | 32 | 3 | Reference | | | Reference | | |
| Thoracic spine | 56 | 14 | 2.882 | 0.828 to 10.04 | 0.096 | 3.714 | 1.016 to 13.58 | 0.047 |
| Lumbar spine | 36 | 9 | 2.899 | 0.784 to 10.71 | 0.111 | 3.958 | 1.036 to 15.12 | 0.044 |
| Sacral spine | 3 | 0 | 0.000 | N/A | 0.997 | 0.000 | N/A | 0.998 |
| **BMI, kg/m²** | | | | | | | | |
| < 18.5 | 8 | 1 | Reference | | | | | |
| 18.5 to 23.9 | 83 | 21 | 2.055 | 0.276 to 15.29 | 0.482 | | | |
| > 23.9 | 36 | 4 | 0.865 | 0.097 to 7.742 | 0.897 | | | |
| **Vertebral body fracture** | | | | | | | | |
| None | 50 | 10 | Reference | | | | | |
| ≤ 50% | 64 | 13 | 1.228 | 0.537 to 2.808 | 0.626 | | | |
| > 50% | 13 | 3 | 1.428 | 0.393 to 5.195 | 0.588 | | | |
| **Laboratory data** | | | | | | | | |
| Normal | 55 | 11 | Reference | | | | | |
| Abnormal | 72 | 15 | 1.350 | 0.618 to 2.949 | 0.451 | | | |
| **Extravertebral metastases** | | | | | | | | |
| No | 67 | 16 | Reference | | | | | |
| Yes | 60 | 10 | 0.729 | 0.331 to 1.608 | 0.434 | | | |
| **Tumour size** | | | | | | | | |
| ≤ 50% body involved | 53 | 10 | Reference | | | | | |
| > 50% body involved | 74 | 16 | 1.275 | 0.578 to 2.811 | 0.547 | | | |
| **Histological type** | | | | | | | | |
| Adenocarcinoma | 101 | 17 | Reference | | | Reference | | |
| Squamous cell carcinoma | 13 | 5 | 2.925 | 1.072 to 7.979 | 0.036 | 4.571 | 1.501 to 13.92 | 0.007 |
| Other | 13 | 4 | 3.097 | 1.026 to 9.347 | 0.045 | 3.488 | 0.945 to 12.87 | 0.061 |
| **ESCC grade** | | | | | | | | |
| < 2 | 9 | 1 | Reference | | | | | |
| ≥ 2 | 118 | 25 | 1.638 | 0.222 to 12.10 | 0.629 | | | |
| **SINS** | | | | | | | | |
| ≤ 12 | 102 | 18 | Reference | | | | | |
| > 12 | 25 | 8 | 2.375 | 1.029 to 5.485 | 0.043 | | | |
| **Revised Tokuhashi score** | | | | | | | | |
| ≤ 8 | 94 | 22 | | | | | | |

(*Continued*)

(*Continued*)

| | | | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|---|---|
| **Variable** | **Regions, n** | **Events, n** | **HR** | **95% CI** | **p-value** | **HR** | **95% CI** | **p-value** |
| > 8 | 33 | 4 | 0.372 | 0.128 to 1.083 | 0.070 | 0.364 | 0.124 to 1.072 | 0.067 |
| **Post-surgical systemic therapy** | | | | | | | | |
| Chemotherapy | 31 | 8 | Reference | | | | | |
| Chemotherapy + targeted therapy | 96 | 18 | 0.647 | 0.281 to 1.488 | 0.305 | | | |
| **Post-surgical radiation** | | | | | | | | |
| No | 84 | 16 | Reference | | | | | |
| Yes | 43 | 10 | 1.066 | 0.483 to 2.354 | 0.875 | | | |

CI, confidence interval; ESCC, epidural spinal cord compression; HR, hazard ratio; N/A, not applicable; SINS, Spine Instability Neoplastic Score.

postoperative systemic therapy, which has achieved remarkable progress and has been widely used in clinics. Given the significant advances in systemic therapies, such as chemotherapy and targeted therapies, which have shown increasing promise in the management of malignancies, including NSCLC, we are concerned about the continued necessity of postoperative radiotherapy in this evolving landscape.

In this study, the prognosis of patients with spinal metastatic NSCLC who received systemic therapy after surgery was analyzed. Based on our results, about 20% of patients developed local progression and about 50% of patients died within three years (see "Clinical outcomes" paragraphs). In our institution, we discovered that most patients adhered well to chemotherapy and targeted therapy, but poorly to radiotherapy. No significant differences in LC or OS were observed between patients with and without post-surgical radiotherapy. Additionally, we found that the improvement in functional outcomes among patients who underwent radiotherapy was not markedly different from those who did not receive this treatment, including the NRS score, KPS score, and mobility. Many previous studies have shown that radiotherapy is important for local tumour control and survival in patients with spinal metastasis.[26–28] However, no study to date has demonstrated whether radiotherapy is of significant importance in improving the prognosis of spinal metastasis in the presence of effective systemic therapy after surgery. In this study, all operations were performed by experienced surgeons with the intent of achieving thorough decompression, and were accompanied by a recommendation for postoperative radiotherapy, ensuring that the influence of surgery on clinical outcomes would be balanced across both study groups. In addition to surgery, all patients in this study received postoperative systemic therapy, mostly within three weeks, which potentially aids in inhibiting local progression while controlling systemic progression. Thus, the effect of radiotherapy in controlling tumour progression appeared to be negligible based on our analysis.

In this study, the histological type of tumour is the only independent prognostic factor for both LC and OS in patients with spinal NSCLC. The predominant subtype of NSCLC in this analysis is adenocarcinoma. A previous study has shown that there is a difference in relapse patterns between NSCLC histological subtypes.[29] Yang et al[30] reported that patients with spinal metastatic lung adenocarcinoma exhibited better prognosis than those with squamous cell carcinoma or unspecified carcinoma. However, according to Zhang and Gong,[31] adenocarcinoma exhibited the shortest survival when compared to other different histological types in bone metastases due to lung cancer. In this study, compared to adenocarcinoma, squamous cell carcinoma and other histological types were associated with worse LC and survival, with and without significant difference, respectively. Further studies are needed to confirm the prognostic correlation of histological types in patients with NSCLC spinal metastasis.

Recent advances in molecular biology have led to the development of novel agents for the treatment of tumour metastases, such as targeted drugs. A substantial improvement in patient outcomes has been achieved after treatments with these targeted agents.[32,33] Target therapy, as an effective systemic therapy, has been reported to play a key role in halting the progression of malignant disease.[34] In our study, about 25% of the lesions received chemotherapy and the remaining 75% were treated with targeted therapy combined with chemotherapy. Patients who received post-surgical targeted therapy plus chemotherapy had significantly better OS than those who received post-surgical chemotherapy only, according to our findings. Consistent with previous studies, targeted therapy appeared to have a significant effect on the survival of spinal NSCLC patients.

Laboratory data have frequently been reported as a key predictor for survival in patients with spinal metastases,[35,36] and have been found to be associated with local recurrence.[37] In the current study, we found that abnormal laboratory data before surgery were associated with a significantly worse OS. The laboratory data here were classified on the basis of the standard at our institution. Our results suggest that restoring patients' laboratory data to normal levels before surgery is crucial for the prognosis of patients with spinal NSCLC.

**Table III.** Results of univariate and multivariate Cox regression analyses of overall survival rate.

| | | | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|---|---|
| **Variable** | **Regions, n** | **Events, n** | **HR** | **95% CI** | **p-value** | **HR** | **95% CI** | **p-value** |
| **Sex** | | | | | | | | |
| Female | 62 | 17 | Reference | | | | | |
| Male | 65 | 30 | 1.914 | 1.052 to 1.480 | 0.033 | | | |
| **Age, yrs** | | | | | | | | |
| < 65 | 80 | 27 | Reference | | | | | |
| ≥ 65 | 47 | 20 | 1.279 | 0.713 to 2.293 | 0.409 | | | |
| **Location** | | | | | | | | |
| Cervical spine | 32 | 12 | Reference | | | | | |
| Thoracic spine | 56 | 19 | 1.375 | 0.661 to 2.857 | 0.394 | | | |
| Lumbar spine | 36 | 15 | 1.230 | 0.566 to 2.671 | 0.601 | | | |
| Sacral spine | 3 | 1 | 1.111 | 0.143 to 8.602 | 0.920 | | | |
| **BMI, kg/m²** | | | | | | | | |
| < 18.5 | 8 | 4 | Reference | | | | | |
| 18.5 to 23.9 | 83 | 28 | 0.544 | 0.190 to 1.562 | 0.258 | | | |
| > 23.9 | 36 | 15 | 0.762 | 0.253 to 2.301 | 0.630 | | | |
| **Vertebral body fracture** | | | | | | | | |
| None | 50 | 20 | Reference | | | | | |
| ≤ 50% | 64 | 23 | 1.316 | 0.718 to 2.410 | 0.374 | | | |
| > 50% | 13 | 4 | 0.885 | 0.301 to 2.603 | 0.824 | | | |
| **Laboratory data** | | | | | | | | |
| Normal | 55 | 17 | Reference | | | Reference | | |
| Abnormal | 72 | 30 | 2.132 | 1.158 to 3.925 | 0.015 | 2.104 | 1.121 to 3.948 | 0.021 |
| **Extravertebral metastases** | | | | | | | | |
| No | 67 | 27 | Reference | | | | | |
| Yes | 60 | 20 | 0.883 | 0.495 to 1.576 | 0.674 | | | |
| **Tumour size** | | | | | | | | |
| ≤ 50% body involved | 53 | 21 | Reference | | | | | |
| > 50% body involved | 74 | 26 | 1.030 | 0.579 to 1.834 | 0.919 | | | |
| **Histological type** | | | | | | | | |
| Adenocarcinoma | 101 | 29 | Reference | | | Reference | | |
| Squamous cell carcinoma | 13 | 12 | 5.033 | 2.530 to 10.01 | < 0.001 | 6.018 | 2.823 to 12.83 | < 0.001 |
| Other | 13 | 6 | 3.344 | 1.359 to 8.224 | 0.009 | 2.503 | 0.863 to 7.261 | 0.091 |
| **ESCC grade** | | | | | | | | |
| < 2 | 9 | 2 | Reference | | | | | |
| ≥ 2 | 118 | 45 | 1.876 | 0.454 to 7.755 | 0.385 | | | |
| **SINS** | | | | | | | | |
| ≤ 12 | 102 | 35 | Reference | | | Reference | | |
| > 12 | 25 | 12 | 2.037 | 1.047 to 3.960 | 0.036 | 1.847 | 0.926 to 3.684 | 0.081 |
| **Revised Tokuhashi score** | | | | | | | | |
| ≤ 8 | 94 | 34 | Reference | | | | | |

(*Continued*)

(*Continued*)

| | | | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|---|---|
| **Variable** | **Regions, n** | **Events, n** | **HR** | **95% CI** | **p-value** | **HR** | **95% CI** | **p-value** |
| > 8 | 33 | 13 | 0.772 | 0.406 to 1.466 | 0.428 | | | |
| **Post-surgical systemic therapy** | | | | | | | | |
| Chemotherapy | 31 | 14 | Reference | | | Reference | | |
| Chemotherapy + targeted therapy | 96 | 33 | 0.392 | 0.207 to 0.743 | 0.004 | 0.450 | 0.211 to 0.960 | 0.039 |
| **Post-surgical radiation** | | | | | | | | |
| No | 84 | 30 | Reference | | | | | |
| Yes | 43 | 17 | 0.897 | 0.494 to 1.630 | 0.721 | | | |

CI, confidence interval; ESCC, epidural spinal cord compression; HR, hazard ratio; SINS, Spine Instability Neoplastic Score.

**Table IV.** Patient-reported outcomes.

| Function | Total | Non-radiotherapy group | Radiotherapy group | p-value* |
|---|---|---|---|---|
| Mean NRS score (SD) | 2.59 (2.84) | 2.78 (2.88) | 2.16 (2.72) | 0.293† |
| Mean KPS score (SD) | 63.7 (17.3) | 63.42 (17.32) | 64.38 (17.59) | 0.797† |
| Mean mobility score (SD) | 4.00 (1.77) | 3.83 (1.86) | 4.41 (1.46) | 0.293† |

*Comparison between the two groups.
†Independent-samples *t*-test.
KPS, Karnofsky Performance Status; NRS, Numerical Rating Scale; SD, standard deviation.

In this study, spinal metastases of NSCLC affected all segments of the spine. They are most common in the thoracic spine, followed by the lumbar spine, cervical spine, and sacral spine. We found that lesions located in the thoracic and lumbar segments were more likely to progress. Furthermore, revised Tokuhashi score > 8 was associated with worse LC without statistical significance. In contrast, SINS showed no significant association with LC in multivariate analysis but appeared to be a key risk factor in univariate analysis. In addition, SINS > 12 was also found to be associated with worse OS, with significant difference in univariate analysis.

Limitations in this study include the retrospective nature and small sample size. Patients included in this study were heterogeneous in terms of histology, radiotherapy, and systemic therapies. In addition, patients were divided into two groups based on the use of radiotherapy without considering different radiation response mechanisms due to the small study cohort. Furthermore, the follow-up period was short, and follow-up visits were irregular, in a small proportion of patients. Finally, we found that post-surgical radiotherapy was not significantly associated with LC and OS in patients with spinal NSCLC metastases in the presence of systemic therapy.

In conclusion, in patients with spinal NSCLC metastasis, tumour histological type was significantly associated with both OS and LC. In the presence of post-surgical systemic therapy, radiotherapy appeared to be less effective in improving LC, OS, or QoL in spinal NSCLC metastasis patients.

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## Data sharing

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