A multicenter, descriptive epidemiologic survey of the clinical features of spinal metastatic disease in China

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Abstract

Background: Spinal metastases have unique epidemiological features and treatment methods. Unfortunately, the relative scarcity of spinal metastases has limited the widespread development of descriptive epidemiological studies, especially in Asian countries. The purpose of this study was to describe the epidemiological characteristics of patients with metastatic spinal tumors in China between 2007 and 2019.

Methods: From January 2007 and July 2019, data on patients with spinal metastases were collected from five cancer centers in China, and demographic characteristics, primary tumor types, segments and numbers of vertebral lesions, disease-related scores, and treatment methods were reviewed.

Results: A total of 2228 patients with spinal metastases were reviewed in this study, including 1279 male patients and 949 female patients, and the male to female ratio was 1.35: 1. More than half of patients developed metastatic diseases between the ages of 50 years and 69 years (64%). Overall, lung cancer (824 cases, 37%) was the most common primary tumor type and the most common level of spinal involvement was multi-level of metastases (860 cases, 39%). 705 patients (32%) had undergone surgical treatments, 1028 patients (46%) had undergone radiotherapy for metastatic vertebrae, and 855 patients (38%) had received systemic treatments. The age, primary tumor type, number of involved vertebrae, Frankel grade, and spinal instability neoplastic score would affect the surgical decision-making.

Conclusions: This study provides insight into the epidemiological characteristics of spinal metastasis and health care service utilization in spinal metastasis patients in China.

Background

With the continuous advancement of diagnostic technology and the prolonged survival of cancer patients, the incidence of spinal metastases in the population is increasing. The spine is the third most common site for distant metastases, behind the lungs and liver [1–3]. Overall, spinal metastases occur in 40%-70% of patients with malignant tumors, and 10%-20% of these patients will experience metastatic spinal cord compression, which is mainly manifested by severe spinal pain, impaired neurological function, and even accelerated process of dying [4–6].

Due to the special anatomical characteristics of the spine, spinal metastases have different epidemiological characteristics and treatment methods compared with metastatic tumors in other anatomic sites. Unfortunately, the relative rarity of spinal metastases has limited the widespread development of descriptive epidemiological studies, especially in Asian countries. Several population-based morbidity and epidemiological surveys have been reported in Western countries [7–9]. Zaikova et al. [7] described the population-based incidence of spinal metastases which required treatment, including patients with or without spinal cord compression, and summarized the neurological function of these patients. The first nationwide epidemiological survey of spinal tumors (including metastatic tumors) in Asia was performed by Sohn and colleagues [10]. They analyzed the age and gender differences, annual
incidence, location of primary tumors, medical costs, and hospital stays associated with spinal tumors in Korea. However, there are few descriptive epidemiological reports on spinal metastases in China, which is undoubtedly unfavorable for providing information to health care institutions and promoting research on spinal metastases.

To identify the epidemiological characteristics of spinal metastases in China, we conducted a descriptive epidemiological survey in five cancer centers throughout the country. By documenting the gender and age, type of primary tumor, site of bone metastases, neurological status, and treatment methods, we expected to provide epidemiological evidence for spinal metastases in China.

**Methods**

**Sources of Data**

The patients in this survey were consecutively recruited from five cancer centers between January 2007 and July 2019. According to the International Classification of Disease, Tenth Revision (ICD-10), we screened cases with complete information through the hospital databases and recorded the patients' gender, age, type of primary tumor, site of bone metastases and other indicators in a unified standard data table.

Inclusion criteria: (1) patients diagnosed with spinal metastases by clinical symptoms, imaging examinations and histopathological examinations; (2) patients with malignant hematological diseases including myeloma and lymphoma; (3) patient with complete medical records.

Exclusion criteria: (1) patients with other spinal diseases, such as bone tuberculosis, osteoporotic fractures, degenerative diseases; (2) patients with primary spinal tumors; (3) outpatients; (4) patients with incomplete data.

**Recorded Indicators**

The medical records were systematically reviewed and the following indicators were recorded: (1) demographic characteristics: age and gender; (2) primary tumor types; (3) segments and numbers of vertebral lesions; (4) disease-related scores: Frankel grade, visual analogue scale (VAS) score, karnofsky performance status (KPS) score and spinal instability neoplastic score (SINS); (5) interventions: surgical treatments and non-invasive treatments.

The Frankel grade is divided into five levels to assess the persistence of sensory and motor functions below the level of injury in cancer patients [11]. The VAS score is used to assess the subjective pain intensity of patients, and is also one of the commonly used indicators for the evaluation of the efficacy after treatment [12]. Assessing the stability of spine requires comprehensive evaluation of imaging and clinical manifestations. The SINS scoring system has a high sensitivity and specificity for potential
unstable spinal lesions, which can help doctors to identify patients who may have spinal instability or deformity [13]. The KPS score can be used to evaluate the general condition of cancer patients. Patients with higher scores can tolerate the side effects of treatments to the greatest extent, and therefore may receive thorough treatments [14].

The management of spinal metastases requires multidisciplinary collaboration, of which surgery and radiotherapy are the main treatment methods. Surgical treatment can be divided into open surgery and minimally invasive surgery. Open surgery includes palliative surgery and radical surgery. Palliative surgery is aimed at alleviating the symptoms of patients and improving the quality of life of patients without pursuing the thoroughness of tumor resection, including laminectomy and vertebra corpectomy. Radical surgery is based on the principle of complete resection of tumor lesions. The goal is to extend the survival time of cancer patients as much as possible, including piecemeal resection and total en bloc spondylectomy. Minimally invasive surgery has the advantages of rapid postoperative recovery, low incidence of complication, and no delay in adjuvant treatment. It is suitable for patients with poor general conditions, including percutaneous vertebroplasty, radiofrequency ablation, and percutaneous pedicle screw fixation.

**Statistical Analysis**

Continuous variables were described as mean ± standard deviation (normal distribution) or median (skewed distribution), and categorical variables were described as frequency or percentage. The Student t-test and chi-square test were used to identify any statistical differences between the means and proportions among the groups. Univariate logistic regression and multivariate logistic regression were used to identify potential factors affecting treatment methods. The variables significant at the p < 0.15 level were included in the multivariate logistic regression analysis to screen out independent predictors. All of the statistical analyses were performed with IBM SPSS Statistics 22.0 (IBM, Armonk, NY, USA) and P < 0.05 (two-sided) was considered statistically significant.

**Results**

**Patient Demographics**

A total of 2228 patients with spinal metastases were reviewed in this study, including 1279 male patients and 949 female patients, and the male to female ratio was 1.35: 1. The average age of onset time of spinal metastases in the general population was 58.6 ± 11.8 years (range 13–92 years), with a median age of 59.0 years. More than half of patients developed metastatic diseases between the age of 50 years and 69 years (63.47%). In terms of subgroups, the mean age of male patients was 59.3 ± 12.3 years (range 14–92 years), with the median age was 60.0 years, and the mean age of female patients was 57.6 ± 11.2 years (range 13–91 years), with the median age was 58.0 years. Using the mean value for analysis, the onset time of female patients was earlier than that of male patients, and the difference was statistically significant (P = 0.001). Further analysis showed that the proportion of elderly patients (over
60 years) in the male population was greater than that of female patients (53.17% vs 47.63%). Similarly, the difference between the proportions was statistically significant (P = 0.012). The distribution of gender and age of patients with spinal metastases was described in Table 1 and Fig. 1.

**Primary Tumor Type**

A study conducted in Korea showed that the six most common primary tumor sites for spinal metastases were lung, liver and biliary tract, breast, colon, stomach and prostate [17]. When subgroup analysis was performed by age, the incidences of lung cancer, liver cancer, colon cancer and gastric cancer were the highest in the 70–79 years age group; in contrast, the incidence of breast cancer was the highest in the age group of 50–59 years age group, and the incidence of prostate cancer was the highest in the over 80 years age group. An epidemiological survey based on a population of spinal metastases in South-East Norway showed that prostate cancer, lung cancer and breast cancer accounted for 66% of all patients, followed by myeloma, lower gastrointestinal tumor, kidney cancer and tumors of unknown origin [7]. Another study comparing trends in surgical treatments of spinal metastases across two decades and three continents noted that colon cancer, liver cancer and lung cancer accounted for a higher proportion in Asian countries, while breast cancer, prostate cancer and myeloma had a lower proportion [18]. The authors believed that the difference was largely dependent on the different high-prevalence cancer types and different early screening programs in different parts of the world.

In the current study, the most common primary tumor was lung cancer, followed by tumors of unknown origin, breast cancer, kidney cancer, and gastrointestinal tumors. For male patients, lung cancer was the most common type, followed by tumors of unknown origin, kidney cancer, prostate cancer, and liver cancer. For female patients, lung cancer was the most common type, followed by breast cancer, tumors of unknown origin, myeloma, and gastrointestinal tumors. This result is partially different from previous literature, especially those based on the population of western countries.

On the one hand, this difference may reflect the significant differences in the incidence of various malignant tumors in different countries, regions and ethnicities. Lung cancer and breast cancer are the most common cancers and the leading causes of cancer death among male and female patients in less developed countries, respectively. However, in more developed countries, prostate cancer is the most common cancer among male patients and lung cancer is the leading cause of cancer death among female patients [19]. In addition, the incidence of liver cancer in China is more than three times than that in North America and 10 times than that of some European countries; while the incidence of breast cancer in China is lower than that in North America [18].

On the other hand, the proportion of tumors of unknown origin in our study reached 16.5%, and the proportion reported in the previous literature were 1.8%-10% [7, 18], which was largely determined by China's national conditions. In some economically underdeveloped areas, some patients who had no history of malignant tumors would refuse further examinations and treatments for primary lesions and only focus on the treatments for spinal lesions, making it difficult to confirm the source of metastatic...
cancer. However, with the enrichment of examination methods and the improvement of economic level, the proportion of tumors of unknown origin had decreased in recent years. Among patients diagnosed in 2015–2019 years, the proportion of tumors of unknown origin were 9.1%-13.3%.

**Spinal Involvement**

The segments and numbers of vertebral lesions in the current study were similar to those in the previous literature [7, 15, 20]. In our study, the most common level of spinal involvement was multi-level metastasis, followed by thoracic vertebrae, lumbar vertebrae, sacral vertebrae, and cervical vertebrae. For 58.98% of patients, the number of involved vertebrae was less than 3.

Bollen and colleagues found that the most common level of spinal involvement was multi-level metastasis, followed by thoracic and lumbar vertebrae, and patients with less than 3 involved vertebrae accounted for 49.57% [15]. In another study conducted by Zaikova and colleagues, based on available radiological records, 83% of patients had multiple lesions, 15% of patients had a single lesion, and 2% of patients were unknown [7]. And they found a statistically significant correlation between the number of metastatic lesions and the type of primary cancer: patients with prostate cancer had the lowest rate of single metastasis (4%), and patients with renal cancer and lymphoma had the highest rate of single metastasis (31% and 47%). For different primary tumors, the distributions of involved vertebrae were similar, with peaks in the lower thoracic and upper lumbar vertebrae.

**Disease-related Scores**

According to the Frankel score, 50.76% of patients (1131 cases) in our study experienced varying degrees of neurological dysfunction, and 49.24% of patients maintained completely normal neurological function. An epidemiological survey of patients with spinal metastases treated with local treatments showed that 40.7% of patients maintained normal neurological function and their neurological status improved over time, with a larger proportion of patients graded as Frankel E. In the 2011–2016 years group, 44.7% of patients had Frankel E grade, while in the 1991–2001 years group, this proportion was only 25.6% [18].

At the time of diagnosis, 77.2% of patients experienced moderate to severe pain, which proves that pain is one of the main symptoms of patients with spinal metastases and patients require external interventions such as radiotherapy, surgery and analgesics. At the same time, only 12.7% of patients experienced inability to take care of themselves or were in a status of severe weakness, requiring special care and assistance. Most patients were in favorable performance status and could tolerate the side effects caused by the treatments to a large extent, so they were more likely to receive thorough treatments, whether invasive or non-invasive.

Although radiotherapy is the cornerstone of palliative treatments of spinal metastases, for more complicated cases such as patients with spinal collapse, kyphosis or scoliosis, and neurological deficits,
the intervention of surgeons may be needed to provide the best treatment outcome. The Spinal Instability Neoplastic Score (SINS) developed by the Spine Oncology Study Group (SOSG) in 2010 can help doctors assess the extent of spinal instability caused by metastatic tumors. In addition [13], the SINS score has been shown to be significantly associated with patient’s survival, spinal adverse events, and pain relief after radiation therapy [21–23]. Although SINS score does not provide recommendations for specific treatment options, it recommended that the patient with a SINS score of 7 or greater should consult a surgeon. In our study, a total of 1797 patients (80.66%) had potential or actual spinal instability at the time of diagnosis and required special attention from surgeons to prevent pain or neurologic deterioration.

**Intervention Measures**

There are many management schemes for spinal metastases, and surgical treatment is an indispensable and important method for the treatment of spinal metastases. The purposes of surgical treatment of spinal metastases are to relieve pain, restore spinal stability, improve neurologic function, control the growth of tumor, improve the quality of life of patients, provide conditions for patients to receive other treatments such as radiotherapy, chemotherapy, and immunotherapy, and even extend the survival [24]. The latest clinical research showed that relatively positive surgical resection and reasonable timing and method of surgery directly affect the quality of life and survival of cancer patients [25, 26]. In the current study, a total of 705 patients (31.64%) underwent surgical treatments, including 154 patients (21.84%) who underwent minimally invasive surgeries, 441 patients (62.55%) who underwent palliative surgeries, and 110 patients (15.60%) who underwent radical surgeries.

In the multivariate analysis that explored factors affecting surgical decision-making, age, primary tumor type, number of involved vertebrae, Frankel grade, and SINS score were five independent predictors. Patients under the age of 60 years and patients with moderate to slow growth speed tumors were more likely to undergo surgery, because these patients have a life expectancy of more than 3 months and are more likely to benefit from surgery [27]. Similarly, a small number of involved vertebrae is also a predictor for favorable prognosis [28]. Patients with spinal instability or metastatic spinal cord compression had a higher chance of receiving surgery because radiation therapy and systemic therapy alone are not sufficient to restore spinal stability and relieve spinal cord compression [13].

In the further subgroup analysis of the surgical population, we found that patients with good neurological function (Frankel E) were three times more likely to undergo minimally invasive surgery rather than open surgery, compared with patients with neurologic deficits. This is a relatively novel conclusion. We speculate that patients with pure pain and good neurological function tend to receive minimally invasive percutaneous vertebroplasty, and those with neurological dysfunction have to choose open decompression surgery, because the minimally invasive pedicle screw fixation combined with minimally invasive decompression in our institutions is relatively rare.
Discussion

The current study identified 2228 patients with spinal metastases, including 1279 male patients and 949 female patients, with a male to female ratio of 1.35:1. In general, the peak incidence was 50-69 years, accounting for 63.47% of the whole population. The mean age of female patients was less than that of male patients, and the difference was statistically significant. Lung cancer was the most common primary tumor type for male and female patients, followed by tumors of unknown origin. When the number of involved vertebrae was less than 3, the lumbar vertebrae were the most common level, and when the number was greater than 3, the multi-level metastases were the most common level. About half of the patients experienced varying degrees of neurological deficits, 80% of the patients experienced potential or actual spinal instability, and 77% of the patients occurred moderate to severe pain. In terms of therapeutic interventions, 31.6% of the patients underwent surgical treatments, 46.1% of the patients underwent radiotherapy, and 38.4% of the patients underwent systemic treatments. Younger patients with tumors of moderate to slow growth speed, less than 3 involved vertebrae, poor neurological function and spinal instability were more likely to receive surgical treatments, while, patients with normal neurological function were more likely to select minimally invasive surgery rather than open surgery.

Patient Demographics

In a large retrospective cohort study of 1043 patients with spinal metastases, the baseline data showed that 542 male patients (52%) and 501 female patients (48%) were included in the study, with a mean age of 64.8 years [15]. Another retrospective study of 544 patients with spinal metastases treated with radiation therapy was performed in Japan, Mizumoto and colleagues [16] reported that there were 287 male patients (52.8%) and 200 female patients (47.2%), with a mean age of 63 years.

Several studies on the epidemiological investigation of spinal metastases also showed that the incidences were higher in male patients than in female patients. In addition, the incidences of spinal metastases increased with age and the proportions of patients in the 60–69 years age group were the highest [10,17].

In the current study, male patients accounted for approximately 57% of the whole population, with a male to female ratio of 1.35:1. The mean age of patients at the time of diagnosis was 58.6 years, and the peak age of onset was 50 to 69 years. Male patients had a larger proportion of elderly patients (over 60 years) compared with female patients (53.2% vs 47.6%), and the difference was statistically significant. The male to female ratio and distribution of age in our study are similar to previous literature. The proportion of male patients is slightly larger than that of female patients, and the mean age at diagnosis is about 60 years. Although there is a statistically significant difference in the age at onset between male patients and female patients, the difference is only 1.7 years, and we think it has little clinical significance. Statistically significant values may be due to the large sample size of the current study.
Limitations

We acknowledge that this study has some limitations. First, due to the retrospective design of this study, selection bias and recall bias are unavoidable. With that in mind, we try to be as inclusive as possible. The study included all consecutive cases that were recorded by specific personnel, and we also tracked cases that were referred through other hospitals or remained in other wards. Second, due to the limited information in our database, we cannot analyze the proportion and grade of spinal cord compression, so we cannot describe the cause of surgical operations, such as emergency spinal cord compression or progressive disease. In the end, the preferred treatment methods for different cancer centers may be different, and the selection criteria for surgical patients were not uniform, which may skew the results. In addition, these data were collected over the span of more than a decade. During this period, the diagnosis and treatment methods of spinal metastases had changed significantly.

Conclusions

The current study provides a relatively detailed epidemiological analysis of patients with spinal metastases in China, and contribute to better understand age and gender differences, primary tumor types, segments and numbers of vertebral lesions, disease-related scores, and independent factors affecting surgical decision-making. Our research provides insight into the epidemiological characteristics of spinal metastasis and health care service utilization in spinal metastasis patients in China.

Abbreviations

ICD-10:International Classification of Disease, Tenth Revision; VAS:Visual Analogue Scale; KPS:Karnofsky Performance Status; SINS:Spinal Instability Neoplastic Score; SOSG:Spine Oncology Study Group

Declarations

Ethics approval and consent to participate: All procedures performed in studies involving human participants were in accordance with the ethical standards of the ethics committee of Tianjin Hospital and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent for publication: Not applicable.

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

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Authors' contributions: HZ analyzed and interpreted the patient data and was a major contributor in writing this manuscript. RQ and XY checked and revised the manuscript. MX collected the data and
sorted out the material. YH participated in the conception of the study and manuscript revision. All authors read and approved the final manuscript.

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Tables

Table 1 Distribution of gender and age in 2228 patients with spinal metastases

| age   | male       | female      | total      |
|-------|------------|-------------|------------|
|       | N          | %           | N          | %           | N          | %           |
| <20   | 5          | 0.39%       | 1          | 0.11%       | 6          | 0.27%       |
| 20-24 | 9          | 0.70%       | 1          | 0.11%       | 10         | 0.45%       |
| 25-29 | 10         | 0.78%       | 12         | 1.26%       | 22         | 0.99%       |
| 30-34 | 17         | 1.33%       | 20         | 2.11%       | 37         | 1.66%       |
| 35-39 | 29         | 2.27%       | 21         | 2.21%       | 50         | 2.24%       |
| 40-44 | 58         | 4.53%       | 45         | 4.74%       | 103        | 4.62%       |
| 45-49 | 102        | 7.97%       | 96         | 10.12%      | 198        | 8.89%       |
| 50-54 | 152        | 11.88%      | 129        | 13.59%      | 281        | 12.61%      |
| 55-59 | 217        | 16.97%      | 172        | 18.12%      | 389        | 17.46%      |
| 60-64 | 239        | 18.69%      | 178        | 18.76%      | 417        | 18.72%      |
| 65-69 | 185        | 14.46%      | 142        | 14.96%      | 327        | 14.68%      |
| 70-74 | 117        | 9.15%       | 77         | 8.11%       | 194        | 8.71%       |
| 75-79 | 84         | 6.57%       | 41         | 4.32%       | 125        | 5.61%       |
| ≥80   | 55         | 4.30%       | 14         | 1.48%       | 69         | 3.10%       |
| total | 1279       | 100.00%     | 949        | 100.00%     | 2228       | 100.00%     |

N: number of patients
Table 2 Distribution of gender and primary tumor types of 2228 patients

| primary tumor type           | male | female | total |
|-----------------------------|------|--------|-------|
|                             | N    | %      | N     | %    | N     | %    |
| lung cancer                 | 483  | 37.76% | 341   | 35.93% | 824   | 36.98% |
| unknown origin              | 218  | 17.04% | 149   | 15.70% | 367   | 16.47% |
| breast cancer               | 1    | 0.08%  | 176   | 18.55% | 177   | 7.94%  |
| kidney cancer               | 117  | 9.15%  | 18    | 1.90%  | 135   | 6.06%  |
| gastrointestinal tumor      | 81   | 6.33%  | 42    | 4.43%  | 123   | 5.52%  |
| myeloma                     | 61   | 4.77%  | 55    | 5.80%  | 116   | 5.21%  |
| liver cancer                | 91   | 7.11%  | 21    | 2.21%  | 112   | 5.03%  |
| prostate cancer             | 97   | 7.58%  | 0     | 0.00%  | 97    | 4.35%  |
| thyroid cancer              | 18   | 1.41%  | 39    | 4.11%  | 57    | 2.56%  |
| sarcoma                     | 21   | 1.64%  | 27    | 2.85%  | 48    | 2.15%  |
| other tumors                | 91   | 7.11%  | 81    | 8.54%  | 172   | 7.72%  |
| total                       | 1279 | 100.00%| 949   | 100.00%| 2228  | 100.00%|

other tumors: lymphoma (n=31), cervical cancer (n=26), melanoma (n=24), bladder cancer (n=21), pancreatic cancer (n=17), cholangiocarcinoma (n=15), ovarian cancer (n=13), adrenal cancer (n=14), skin cancer (n=6), carcinoma of testis (n=2), carcinoma of penis (n=2), nasopharynx cancer (n=1)

Table 3 Distribution of segments and numbers of involved vertebrae

| level of spinal involvement | <3  | %   | ≥3  | %   |
|-----------------------------|-----|-----|-----|-----|
| cervical vertebrae          | 115 | 8.75% | 30  | 3.28% | 145  | 6.51% |
| thoracic vertebrae          | 426 | 32.42% | 160 | 17.51% | 586  | 26.30% |
| lumbar vertebrae            | 428 | 32.57% | 60  | 6.56%  | 488  | 21.90% |
| sacral vertebrae            | 149 | 11.34% | 0   | 0.00%  | 149  | 6.69%  |
| multi-level                 | 196 | 14.92% | 664 | 72.65% | 860  | 38.60% |
| total                       | 1314 | 100.00% | 914 | 100.00% | 2228 | 100.00% |

multi-level of metastases: involve two or more segments of cervical vertebra, thoracic vertebra, lumbar vertebra, and sacral vertebra at the same time; sacral vertebrae: due to inconsistency in radiographic records of different medical centers, the sacral vertebrae and caudal vertebra were defined as one vertebra
| variables                                      | number | univariate analysis | multivariate analysis |
|-----------------------------------------------|--------|---------------------|-----------------------|
| gender                                       |        |                     |                       |
| male patient                                 | 1279   | ref                 |                       |
| female patient                               | 949    | 1.073 0.459         |                       |
| age                                          |        |                     |                       |
| ≤60y                                         | 1136   | ref                 | ref                   |
| >60y                                         | 1092   | 0.642 <0.001        | 0.696 0.571-0.848 <0.001 |
| type of primary tumor by growth speed        |        |                     |                       |
| fast                                         | 1455   | ref                 | ref                   |
| moderate and slow                            | 773    | 1.261 0.018         | 1.457 1.188-1.787 <0.001 |
| number of involved vertebrae                 |        |                     |                       |
| <3                                           | 1314   | ref                 | ref                   |
| ≥3                                           | 914    | 0.448 <0.001        | 0.416 0.338-0.512 <0.001 |
| Frankel grade                                |        |                     |                       |
| A-D                                          | 1131   | ref                 | ref                   |
| E                                            | 1097   | 0.488 <0.001        | 0.498 0.410-0.606 <0.001 |
| KPS score                                    |        |                     |                       |
| ≤70                                          | 1395   | ref                 |                       |
| >70                                          | 833    | 1.143 0.259         | NI                    |
| SINS score                                   |        |                     |                       |
| 0-6                                          | 431    | ref                 | ref                   |
| 7-12                                         | 1439   | 1.614 <0.001        | 1.621 1.245-2.110 <0.001 |
| 13-18                                        | 359    | 1.803 <0.001        | 1.895 1.356-2.649 <0.001 |
| VAS score                                    |        |                     |                       |
| 0-3                                          | 508    | ref                 |                       |
| 4-6                                          | 980    | 1.128 0.442         |                       |
| 7-10                                         | 740    | 1.014 0.562         | NI                    |

NI: not included
| Variables                                  | number | Univariate analysis | Multivariate analysis |
|--------------------------------------------|--------|---------------------|-----------------------|
| **gender**                                 |        |                     |                       |
| Male patient                               | 395    | ref                 |                       |
| Female patient                             | 310    | 1.117 0.547         | NI                    |
| **age**                                    |        |                     |                       |
| ≤60y                                       | 324    | ref                 |                       |
| >60y                                       | 381    | 0.898 0.555         | NI                    |
| **type of primary tumor by growth speed**  |        |                     |                       |
| Fast                                       | 434    | ref                 |                       |
| Moderate and slow                          | 271    | 0.959 0.823         | NI                    |
| **number of involved vertebrae**           |        |                     |                       |
| <3                                         | 489    | ref                 |                       |
| ≥3                                         | 216    | 0.917 0.666         | NI                    |
| **Frankel grade**                          |        |                     |                       |
| A-D                                        | 447    | ref                 | ref                   |
| E                                          | 258    | 2.787 <0.001        | 2.941 1.934-4.474 <0.001|
| **KPS score**                              |        |                     |                       |
| ≤70                                        | 393    | ref                 | ref                   |
| >70                                        | 312    | 1.486 0.030         | 0.895 0.588-1.361 0.604|
| **SINS score**                             |        |                     |                       |
| 0-6                                        | 103    | ref                 |                       |
| 7-12                                       | 472    | 1.212 0.563         |                       |
| 13-18                                      | 130    | 0.878 0.690         | NI                    |
| **VAS score**                              |        |                     |                       |
| 0-3                                        | 127    | ref                 |                       |
| 4-6                                        | 334    | 1.330 0.275         |                       |
| 7-10                                       | 244    | 1.134 0.648         | NI                    |

NI: not included

**Figures**
Figure 1

Distribution of gender and age of patients with spinal metastases. More than half of patients developed metastatic diseases between the age of 50 years and 69 years. The mean age of male patients and female patients was 59 years and 58 years, respectively.
Figure 2

Distribution of gender and primary tumor types of patients with spinal metastases. Lung cancer was the most common primary tumor type, followed by tumors of unknown origin, breast cancer, and kidney cancer, etc.
Figure 3

Changes in the proportion of primary tumor types from 2010 to 2019. The proportion of tumors of unknown origin was decreasing year by year, from 25.5% in 2010 to 9.1% in 2019; at the same time, the proportions of other tumor types had not changed significantly.