

Original Article

Postoperative survival and functional outcome of palliative decompression and stabilization for thoracic metastatic spinal cord compression: prognostic factor analysis

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Abstract: Objective: To analyze the survival time and functional outcome of patients with thoracic metastatic spinal cord compression (MSCC) after operation and to identify parameters influencing the postoperative survival time. Methods: Sixty-seven consecutive patients with thoracic MSCC who were performed with posterior decompression and spine stabilization from January 2010 to December 2014 were retrospectively in this study. Nine prognostic factors, namely, age, primary tumor, preoperative Eastern Cooperative Oncology Group (ECOG) performance status, interval from cancer diagnosis to spinal metastases, preoperative ambulatory status, preoperative visceral metastases, number of extraspinal bone metastasis, number of involved vertebrae, and postoperative adjuvant radiotherapy, were investigated. All factors were analyzed by Kaplan-Meier method and Cox proportional hazards model. Results: Postoperative Frankel grade was improved in 52% patients, maintained in 43% and retrogressive in 5%. Postoperative ambulatory rate was significantly higher than the preoperative ambulatory rate ($P < 0.001$). VAS score decreased from preoperative 5.7 ± 1.7 to postoperative 2.1 ± 1.4 score ($P < 0.01$). Surgery-related complications occurred in 13.4% (9/67) patients. In the multivariate Cox regression analysis, age, type of primary tumor, preoperative visceral metastases, preoperative ECOG-PS, and postoperative adjuvant radiotherapy were independent prognostic factors for survival in patients with MSCC after surgery. Conclusions: Posterior decompression and stabilization is a relatively safe and effective method for MSCC. Besides, our study showed that age, type of primary tumor, preoperative visceral metastases, preoperative ECOG-PS, and postoperative adjuvant radiotherapy were independent characteristics for postoperative survival.

Keywords: Spinal metastasis, metastatic spinal cord compression, surgery, prognostic factor

Introduction

Metastatic spinal cord compression (MSCC) is one of the most serious complications of spinal metastases which occurs in approximately 10% to 20% patients with advanced cancer [1]. Seventy percent patients with MSCC occur in the thoracic vertebrae [2]. Local pain is usually the earliest symptom, and patients may suffer from neurological dysfunction as the disease progresses, which may lead to the interruption of combined treatments for those patients. Stu-

dies showed that once patients totally paralyzed, neurological function would be difficult to recover as before [3-5].

The expected survival time of patients with MSCC is usually short. The median survival period is 2-6 months according to reports in the literatures [2]. Therefore, the goals of treatment for MSCC are alleviating the pain, preventing or improving neurological dysfunction and improving the quality of life. Postoperative outcome prediction can help physicians to choose the

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Table 1. Univariate analysis of survival

Parameters	Number of Patients	Median survival (days)	95% CI	P value
Age				
< 65 years	43	366	275-457	0.000
≥ 65 years	24	156	106-206	
Preoperative ECOG score				
1-2	31	474	280-668	0.000
3-4	36	186	168-204	
Primary tumor				
Lung	29	180	140-220	0.000
Liver	10	160	104-216	
Renal	8	414	165-663	
Prostate	5	474	90-857	
Breast	15	750	215-1285	
Preoperative ambulatory status				
None	34	192	171-213	0.201
Yes	33	345	173-517	
Visceral metastases				
None	33	414	344-483	0.000
Yes	34	160	130-190	
Extraspinal bone metastases				
None	24	321	137-505	0.202
Yes	43	222	143-301	
Number of spine metastases				
1-2	43	378	285-470	0.000
≥ 3	24	153	101-205	
Interval from cancer diagnosis to spinal metastases				
< 24 months	53	201	168-234	0.000
≥ 24 months	14	861	218-1504	
Postoperative adjuvant radiotherapy				
None	27	174	144-204	0.000
Yes	40	420	355-485	

Annotation: ECOG, Eastern Cooperative Oncology Group; 95% CI, 95% confidence interval; P value, Log-rank test.

appropriate treatment, such as supportive care, palliative radiotherapy, palliative surgery and excisional surgery. The treatment strategy of MSCC is multidisciplinary and individualization. Surgery should be performed in an appropriate time so that the radiotherapy or chemotherapy wouldn't be delayed. Prognostic scoring system is used to help clinician timely and accurately formulate an effective therapeutic strategy and to avoid excessive treatment and inadequate treatment. This study retrospectively analyzed clinical and imaging data of 67 patients with thoracic MSCC, our objective was to present the postoperative survival and functional outcome of patients with thoracic MSCC after operation and to identify parameters that might have influence the postoperative survival.

Materials and methods

Inclusion and exclusion criteria

Inclusion criteria: (1) Patients were diagnosed with thoracic MSCC. (2) Patients were treated with posterior decompression and stabilization. (3) Expected survival was over 3 months. Exclusion criteria: (1) Primary spinal malignant tumor. (2) Intramedullary metastases. (3) Lesions were previously treated by surgery or radiotherapy. (4) Lost to follow-up.

Characteristics of patients

The entire cohort of 67 consecutive patients (145 vertebrae) treated with posterior decompression and stabilization for thoracic MSCC

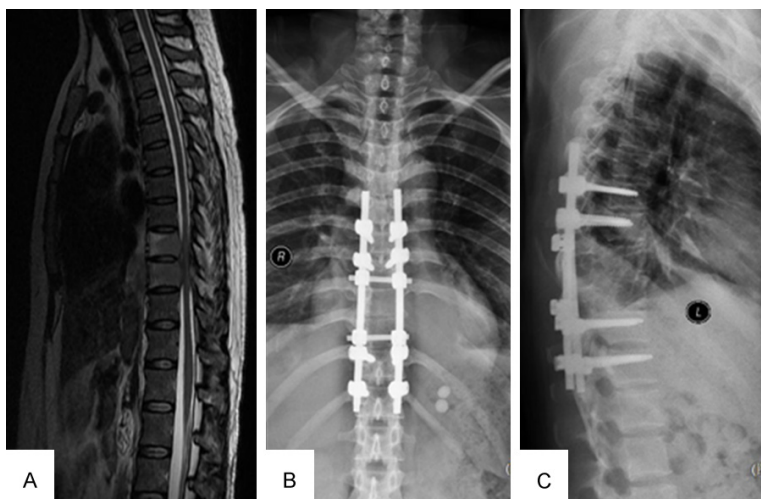


Figure 1. 43-year-old female, T9 and T10 vertebral metastasis of breast cancer. Preoperative Frankel grade was D. Frankel grade was E after surgery. Survival time was 750 days. Preoperative magnetic resonance imaging (MRI) showed spinal metastasis of T9-10 vertebrae and spinal cord compression (A). Postoperative X-ray film (B and C).

were enrolled in our study. There were 31 females and 36 males with a mean age of 57 ± 11 years (range, 32-76 years). The primary tumour was lung cancer in 29 (43%) patients, breast cancer in 15 (22%) patients, liver cancer in 10 (15%) patients, renal cancer in 8 (12%) patients, and prostate cancer in 5 (8%) patients. One thoracic vertebra was invaded in 23 (34%) patients, two were invaded in 20 (30%) patients, 3 or more were invaded in 24 (36%) patients (**Table 1**). Tokuhashi score was 0 to 8 points in 36 (54%) patients, 9 to 11 points in 20 (30%) patients, and 12 to 15 points in 11 (16%) patients.

The ECOG-PS was used to evaluate patient's general condition. Visual analog score (VAS) was used to evaluate pain intensity. Frankel grade, ranging from A to E, was used to evaluate neurological dysfunction. The following data should be collected, such as gender, age, type of primary tumor, preoperative ECOG-PS, interval from cancer diagnosis to spinal metastases, preoperative ambulatory status (patients with Frankel D to E are ambulatory), preoperative visceral metastases, number of extra-spinal bone metastasis, number of involved vertebrae, postoperative adjuvant radiotherapy, preoperative and postoperative VAS score, and preoperative and postoperative Frankel grade. The Medical Research Ethics Board of the 307 th hospital of the Chinese People's Liberation Army approved this retrospective

study and required neither patient approval nor informed consent for review of patients' images and medical records.

Surgery

Neurological deficit caused by MSCC (sensory and/or motor function impairment, sphincter dysfunction) was the major indication for posterior laminectomy decompression (with or without partial vertebrectomy) and stabilization (**Figure 1**). Postoperative local radiotherapy was performed 2-3 weeks after the operation. All the treatments were decided by oncologists, radiologists and orthopedic surgeons.

Statistical analysis

We used SPSS 18.0 software (SPSS Institute, Chicago, USA) for the statistical analyses. Continuous quantitative variables were described as mean \pm standard deviation. Kappa consistency test was used to evaluate the level of agreement between the survival time predicted by the Tokuhashi score and the observed survival time. Prognostic factors were analyzed by Kaplan-Meier and Cox proportional hazards analysis. In all analyses, a value of $P < 0.05$ was considered to be statistically significant.

Results

Survival and functional outcome

The average follow-up time was 11.7 ± 10.7 months (range, 0.3-52.8 month). At the end of follow-up (May 31, 2015), ten (15%) patients were still alive, and the overall median survival time was 10.8 months (95% CI, 7.3-14.3 months). Two (3%) patients died within a month after surgery due to pulmonary embolism (1 patient) and severe pulmonary infection (1 patient). Forty-five (67%) patients died within one year. Sixty (82%) patients died within two years.

Twenty-nine patients were nonambulatory before operation. Seventeen patients (59%) regained the ability to walk after operation. However, two patients (5%) who were ambulatory before

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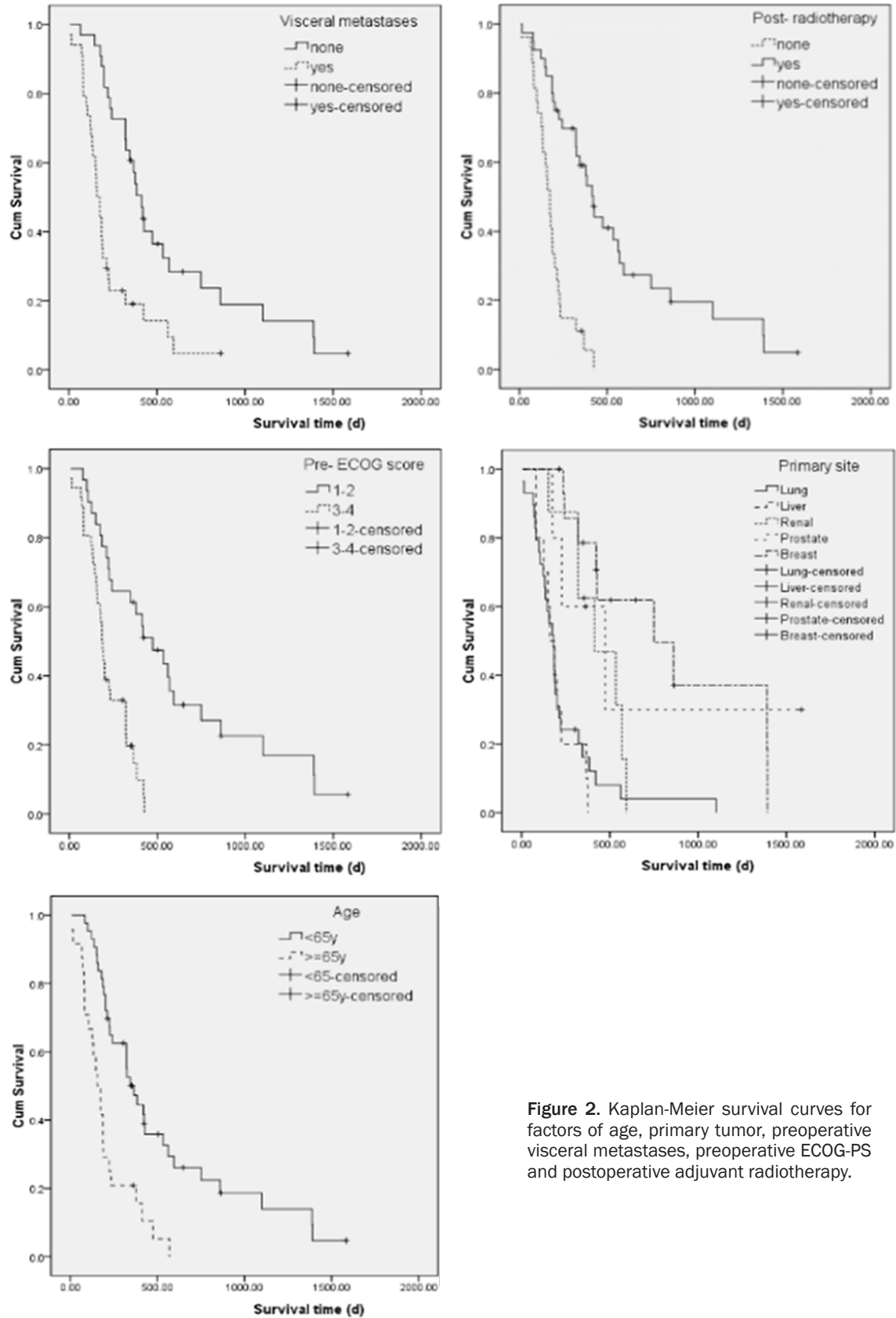


Figure 2. Kaplan-Meier survival curves for factors of age, primary tumor, preoperative visceral metastases, preoperative ECOG-PS and postoperative adjuvant radiotherapy.

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Table 2. Multivariate analysis of survival

Parameters	P value	Relative risk	95% CI for RR
Age	0.012	2.484	1.217-5.072
Primary tumor	0.000	0.624	0.499-0.781
Visceral metastases	0.002	2.601	1.402-4.825
Preoperative ambulatory status	0.562	1.292	0.544-3.067
Preoperative ECOG score	0.013	1.837	1.137-2.966
Interval from cancer diagnosis to spinal metastases	0.674	0.864	0.437-1.708
Number of spine metastases	0.699	1.077	0.738-1.573
Extraspinal bone metastases	0.194	1.502	0.813-2.775
Postoperative adjuvant radio-therapy	0.021	0.450	0.228-0.888

Annotation: ECOG, Eastern Cooperative Oncology Group; 95% CI, 95% confidence interval; RR, Relative Risk.

Table 3. Observed survival and survival predicted by the Tokuhashi score of 57 dead patients at last follow-up

Survival predicted by the Tokuhashi score (months)	Observed survival (months)			Total
	< 6	6-12	> 12	
< 6	9	2	-	11
6-12	2	24	8	34
> 12	-	1	11	12
Total	11	31	15	57

operation lost their ability to walk due to death within a month. Postoperative Frankel grade was improved in 52% (35/67) patients, maintained in 43% (29/67) and retrogressive in 5% (3/67). Preoperative and postoperative ambulatory status had statistical significance ($P < 0.001$, chi-square test). VAS score decreased from preoperative 5.7 ± 1.7 score to postoperative 2.1 ± 1.4 score ($P < 0.01$, Wilcoxon signed-rank test). Surgery-related complications occurred in 13.4% (9/67) patients.

Identification of prognostic factors of survival

In univariate analysis (Kaplan-Meier, log-rank test), age ($P < 0.01$), primary tumor ($P < 0.05$), preoperative ECOG-PS ($P < 0.01$), interval from cancer diagnosis to spinal metastases ($P < 0.01$), preoperative visceral metastases ($P < 0.01$), number of spine metastases ($P < 0.01$) and postoperative adjuvant radiotherapy ($P < 0.01$) significantly affected the postoperative survival. But in the multivariate analysis, age ($P = 0.012$), primary tumor ($P = 0.000$), preoperative visceral metastases ($P = 0.002$), preoperative ECOG-PS ($P = 0.013$) and postoperative adjuvant radiotherapy ($P = 0.021$) were important prognostic factors for survival in patients with MSCC (**Figure 2** and **Table 2**).

Performance of Tokuhashi score

The distribution of fifty-seven dead patients was as follows (**Table 3**): score 0-8 (predicted survival time < 6 months), 19% (11/57) patients, score 9-11 (> 6 months but < 12 months), 60% (34/57) patients, and score 12-15 (> 12 months), 21% (12/57) patients. Observed median survival of the three groups was 5.3 months (95% CI, 4.4-6.2 months), 13.6 months (95% CI, 10.1-15.1 months), 25 months (95% CI, 14.1-41.8 months), respectively. Observed survival was consistent with the survival predicted by Tokuhashi score via Kappa consistency test ($Kappa = 0.626$, $P < 0.001$).

Discussion

Patients with spinal metastasis, which often occurred in the patients with advanced cancer, usually have a short life expectancy, and the purpose of treatment is mainly to improve the neurological function, relieve pain, and improve the quality of life at last. In 1976, a prospective trial showed that patients managed with radiotherapy and laminectomy had no significant outcome differences compared with patients managed with radiotherapy alone [6]. After a period of time, the role of surgery for spinal metastases was controversial. However, the controversy was stopped not until a prospective randomized study performed by Patchell et al. in 2005 [7]. This study showed that outcomes of patients with surgery and radiotherapy were significantly better than radiotherapy alone. At present, surgery is essential for spinal metastases to relieve spinal cord compression and improve stability. In our study, postoperative Frankel grade was improved or maintained in 52% and 43% patients, respectively.

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The commonly used surgical procedures include excisional surgery, palliative decompression and minimally invasive surgery. A study showed a long survival in patients with excisional surgery. But the incidence of complications was as high as 20% [8]. Nowadays, palliative decompression is still the standard surgical procedure for MSCC. Surgery strategy should be individualized and multidisciplinary. Individual treatment strategy is often based on the patient's survival and functional prognosis. Generally speaking, excisional surgery was considered for patients whose survival was greater than 12 months. Patients with very short survival time and poor functional outcome shouldn't be the candidates for decompressive surgery. So patients with difference prognosis had difference treatment strategy. An accurate prognostic scoring system can help clinicians to develop individualized treatment plan, avoiding excessive medical treatment and insufficient treatment.

In 1990, Tokuhashi et al. developed a prognostic scoring system, Tokuhashi score, then was revised in 2005 [9, 10]. Finally, six prognostic factors were included: primary tumor, Karnofsky performance status, metastases to major internal organs, number of extraspinal bone metastases, number of spinal metastases and Frankel grade. Tomita score was developed by Tomita in 2001, and was revised by Kawahara et al. in 2009 [11, 12]. This score system contains three prognostic factors: primary tumor, metastases to major internal organs, bone metastases. Many Studies have confirmed the validity of revised Tokuhashi and Tomita score as a prognostic tool for patients with spinal metastases [13-16]. However, they are not impeccable. In 2012, Popovic et al. [17] reviewed previous scoring system, such as revised Bauer score, revised Tokuhashi score, revised Tomita score, van er Linde and Sioutos scoring system. They thought that none of these scoring system was applicable to all types of patients with spinal metastases.

In our study, survival predicted by the Tokuhashi score had good consistency with the observed survival ($P < 0.001$). It also indirectly showed that palliative surgery has no improvement on survival. In the univariate analysis, age (< 65 years), breast and prostate cancer, preoperative ECOG (1-2), interval from cancer diagnosis to spinal metastases (< 24 months), visceral metastases (none), number of spine metastases

(1-2) and postoperative adjuvant radiotherapy were associated with longer postoperative survival. But in the multivariate analysis, age ($P = 0.012$), primary tumor ($P = 0.000$), visceral metastases ($P = 0.002$), preoperative ECOG-PS ($P = 0.013$) and postoperative adjuvant radiotherapy ($P = 0.021$) were independent prognostic factors of survival of MSCC after thoracic posterior decompressive surgery. Thus, besides Tokuhashi score (primary tumor, Karnofsky performance status, metastases to major internal organs, number of extraspinal bone metastases, number of spinal metastases and Frankel grade), age and postoperative adjuvant radiotherapy were also important prognostic factors of postoperative survival.

In conclusion, posterior decompression and stabilization is an safe and effective means for MSCC. Our study supports the validity and reproducibility of the Tokuhashi score. Moreover, age and postoperative adjuvant radiotherapy were also significantly associated with postoperative survival in our population.

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Disclosure of conflict of interest

None.

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