

## Efficacy of Tokuhashi Score in Predicting the Prognosis among Chinese Patients with Spinal Metastasis

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**Abstract:** Objective: To investigate the effectiveness of the Tokuhashi score in predicting the prognosis among Chinese patients with spinal metastasis who underwent the surgeries. Methods: A total of 109 patients with spinal metastasis underwent the surgeries between 2008 and 2018 were enrolled in this study. Rank correlation was used to assess the relationship between Tokuhashi score and the actual survival time. Log-Rank test was used to analyze the survival data. A univariate survival analysis was carried out using the Kaplan-Meier method. Results: There were 68 cases at score 0-8, 37 at score 9-11 and 4 at score 12-15 on the basis of Tokuhashi score. Our findings showed no statistical differences in the actual survival time ( $R=0.111$ ,  $P=0.253$ ) and median survival time ( $P=0.326$ ) among the three scoring groups. The median survival time of score 0-8 was 10.90 (95%CI: 6.40-13.80) months, of score 9-11 was 13.90 (95%CI: 6.20-26.20) months, and of score 12-15 was 59.80 (95%CI: 5.40-59.80) months. Conclusion: Tokuhashi score may be not an accurate tool for predicting the prognostic survival in Chinese patients with spinal metastasis.

### 1. Introduction

Spine, a common site for metastasis to the skeletal system, is the third metastatic segment following lung and liver [1], accounting for about 50% [2, 3]. A previous study reported that approximately 5%-10% of cancer patients suffered from spinal metastasis [4-7]. It is characterized by the gradually aggravated localized pain including haphalgnesia and percussed pain. Nearly 5%-10% patients may undergo the spinal compression that manifests the symptoms of intractable pain, neurological deficit and spinal instability during the disease process [8, 9]. At present, the surgical treatments are major options supplemented by radiotherapy for spinal metastasis in clinic [10], improving the quality of life. Although the survival of patients with cancers has been prolonged [11], the frequency of metastases is also simultaneously increased. Therefore, it is necessary to pay close attention to the prognosis of the patients after surgery.

To help the surgeons protocol the appropriate treatment strategies, predictive systems have been developed to postoperatively assess the life expectancy of patients. Tokuhashi score, an original scoring system, was first proposed by Tokuhashi et al in 1990 [12], and modified in 2005 [13], which has been widely used for the prognostic assessment of spinal metastasis worldwide. Early studies showed that Tokuhashi score may be an effective tool for estimating the survival time of patients with secondary spine metastasis after surgery in several countries, such as America, Denmark and Korea, which facilitates doctors to determine preoperative indications and therapeutic schedules. To the best of our knowledge, however, the application of this scoring system for the prognostic predication among Chinese patients has rarely reported.

In the current study, we investigated the effectiveness of the Tokuhashi score in predicting the prognosis of Chinese patients with spinal metastasis via evaluating the association between the scoring system and actual survival time observed from surgical patients.

## 2. Methods

### 2.1 Patients

A total of 109 Chinese patients who had undergone the surgeries for spinal metastasis admission to Shenzhen People's Hospital between 2008 and 2018 were enrolled in this study. All patients received the clinical, neurologic, laboratory and radiologic examinations. The information including age, gender, surgical approach, general condition, metastasis, nervous state and primary site were recorded. This study was approved by the Institutional Review Board (IRB) of Shenzhen People's Hospital (the approval number: No.LL-KY-2019535).

Inclusion criteria were: (1) patients with spinal metastasis who underwent the surgeries, (2) age  $\geq 18$  years, and (3) at least 1-year follow-up. Exclusion criteria were: (1) patients without histologic confirmation of the spinal lesion, and (2) loss to follow-up.

### 2.2 Surgical Technique

If the manifestations of radiology and neurology of patients were consistent, the operations were performed according to at least one features: spinal instability, progressive deformity, symptomatic spinal cord compression with progressive neurologic deficit, intractable pain, tumor resistance to radiotherapy and chemotherapy. The surgical strategies were percutaneous vertebroplasty combined with percutaneous kyphoplasty (PVP&PKP) or spinal nerve decompression. Pedicle screws were used to stabilize in the presence of instability.

### 2.3 Tokuhashi Score

Postoperative modified Tokuhashi scores were established based on medical records. Six parameters of the score were the general condition, number of extraspinal bone metastases, number of metastases in the vertebral bone, metastases to major internal organs, the primary site of the cancer and the severity of spinal cord palsy. The actual survival duration was presented as the patients' survival which was assessed using Tokuhashi score [13, 14] (Table 1). According to the scores and prognosis for survival, patients were divided into the following groups: (1) 0-8 points, <6 months of survival; (2) 9-11 points, 6-12 months of survival; and (3) 12-15 points, survival >12 months.

Table 1 Modified Tokuhashi Score

Parameters	Score=0	Score=1	Score=2	Score=3	Score=4	Score=5
General condition	10%-40%	50%-70%	80%-100%			
Extraspinal bone metastasis	>2	$\leq 2$	0			
Metastasis in the vertebral bone	>2	$\leq 2$	0			
Visceral metastasis	Non-removable	Removable	None			
Primary site	Lung, osteosarcoma, stomach, bladder esophagus, pancreas	Liver, gallbladder	Others	Kidney, uterus	Rectum	Thyroid, breast, prostate carcinoid tumor
Palsy	Frankel A, B	Frankel C, D	Frankel E			

### 2.4 Statistical Analysis

Statistical analyses were performed using SAS 9.4. Categorical data were presented as n (%) and analyzed using  $\chi^2$  tests. The relationship between Tokuhashi score and actual survival time was analyzed by Rank correlation. The survival data were analyzed using Log-Rank test. A univariate survival analysis was carried out using the Kaplan-Meier method. *P*-value <0.05 was considered statistically significant.

### 3. Results

#### 3.1 The Baseline Characteristics of Patients Underwent Surgeries for Spinal Metastasis

In total, numbers of patients were 109 with the mean age of (56.68±14.99) years. Of these, the average age of 66 males (60.55%) was (56.94±14.85) years, and of 43 females (39.45%) was (56.28±15.36) years. According to the surgical methods, 49 patents (44.95%) were treated using the PVP&PKP, and 60 cases were cured by the decompression (55.05%) groups. For the severity of spinal cord palsy, 76 cases were classified as Frankel E (69.72%). The characteristics of patients with spinal metastasis who underwent surgeries were shown in Table 2.

Table 2 the Characteristics Of Patients with Spinal Metastasis Who Underwent Surgeries

Variables	n	%
Total	109	
Age	56.68±14.99	
Gender		
Male	66	60.55
Female	43	39.45
Surgical approach		
PVP+PKP	49	44.95
Decompression	60	55.05
General condition		
KPS 10%-40% (score=0)	14	12.84
KPS 50%-70% (score=1)	25	23.85
KPS 80%-100% (score=2)	70	63.30
Extraspinal bone metastasis		
>2 (score=0)	23	21.10
≤2 (score=1)	31	28.44
0 (score=2)	55	50.46
Metastasis in the vertebral bone		
>2 (score=0)	65	59.63
≤2 (score=1)	44	40.37
0 (score=2)	0	0.00
Visceral metastasis		
Non-removable (score=0)	30	27.52
Removable (score=1)	6	5.50
None (score=2)	73	66.97
Palsy		
Frankel A, B (score=0)	8	7.34
Frankel C, D (score=1)	25	22.94
Frankel E (score=2)	76	69.72
Primary site		
Lung, osteosarcoma, stomach, bladder, esophagus, pancreas (score=0)	49	44.95
Liver, gallbladder, unknown (score=1)	16	14.68
Others (score=2)	27	24.77
Kidney, uterus (score=3)	4	3.67
Rectum (score=4)	0	0.00
Thyroid, breast, prostate, carcinoid (score=5)	13	11.93

#### 3.2 Association between Survival Time and Tokuhashi Score

The association between survival time and Tokuhashi score was listed in Table 3. There were 68 cases at score 0-8, 37 at score 9-11 and 4 at score 12-15 on the basis of Tokuhashi score. There were no statistical differences in the actual survival time among the three groups (R=0.111, P=0.253). It was indicated that the Tokuhashi score may not predict the actual survival time.

Table 3 Tokuhashi Score Stratified by Actual Survival

Tokuhashi score	n	Actual survival (months)	S	P
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		<6	6-12	>12		
0-8	68	24 (68.57)	10 (66.67)	34 (57.63)	53.114	<0.001
9-11	37	10 (28.57)	5 (33.33)	22 (37.29)		
12-15	4	1 (2.86)	0 (0.00)	3 (5.08)		

### 3.3 Tokuhashi Score Stratified by Actual Survival

In Table 4, the results showed that no differences in median survival time among three groups ( $P=0.326$ ). The median survival time of score 0-8 was 10.90 months (95%CI: 6.40-13.80), of score 9-11 was 13.90 months (95%CI: 6.20-26.20), and of score 12-15 was 59.80 months (95%CI: 5.40-59.80).

Table 4 the Median Survival Time of the Three Groups

Tokuhashi score	n	Median survival (months)	95%CI	<i>P</i>
				0.326
0-8	68	10.90	6.40-13.80	
9-11	36	13.90	6.20-26.20	
12-15	5	59.80	5.40-59.80	

## 4. Discussion

Spinal metastasis, a usual symptom of bone metastasis, is a growing concern in clinical treatments. Approximately 20-40% of cancer patients develop vertebral metastatic diseases before the end of life, of which 20% suffer from neurological symptoms owing to the compression of epidural spinal cord. Surgery is an important treatment for spinal metastatic tumor, and its purpose is to relieve the patients' pain, relieve nerve compression, control tumor progression and rebuild spinal stability. However, the majority of patients with spinal metastasis are in advanced stage, with short survival time and complex disease condition. Currently, there are no uniform standards for the selection of operation timing and therapeutic protocols due to the lack of objective and quantitative comprehensive assessment systems.

With the development of chemotherapy, radiotherapy, targeted therapies and immunotherapy, the overall survival of malignant tumors has been prolonged. Survival estimation has been gradually utilized to determine therapeutic options for spinal metastasis in clinic. To date, there are several scoring systems for estimating the expected survival time of spinal metastasis patients, including Tokuhashi [12], revised Tokuhashi [15-17], Tomita [14], Bauer [18] and revised Bauer [19] scores. Among these scores, the revised Tokuhashi score is a most common scoring, which can predict the prognosis of spinal metastasis to provide the basis for treatment selection. In this study, we investigated the effectiveness of the Tokuhashi score in predicting the prognosis of Chinese patients with spinal metastasis via assessing the association between the scoring system and actual survival time observed from surgical patients.

Tokuhashi et al found the consistency was up to 86.4% between the predicted prognosis and the actual survival among 118 patients [13]. The previous study reported that the actual survival time of 67 cases (79%) was matched with the expected survival time among 85 patients assessed by the revised Tokuhashi score [20]. Nevertheless, our findings showed no statistical differences in the actual survival time in three groups of score 0-8, 9-11 and 12-15. The median survival time of score 0-8 was 10.90 months, of score 9-11 was 13.90 months, and 59.80 months. It was indicated that the revised Tokuhashi score may not predict the actual survival time. Similarly, some scholars suggested that the score performed a low level for the survival prediction [21]. Gakhar et al demonstrated that the prediction of the score was effective in survival time >12 months, but not in <1 month or 6-12 months [22]. Although the revised score has been proved to be practicable and accurate for predicting the life expectancy of patients with spinal metastasis in plenty of former studies as well as the current study, it was also limited since it had only analyzed the prognostic effect of preoperative characteristics, which may explain our findings.

Limitations of this study should be reported. The participants were recruited in one center and

only those who underwent surgeries for spinal metastasis may reduce the statistical power, so that the generalization should be cautious. Future studies with large sample and multicenter are needed to assess the predictive effectiveness of Tokuhashi score in the survival time among Chinese patients with spinal metastasis.

## 5. Conclusion

In the current study, we investigated the predictive efficacy of Tokuhashi score in the survival of spinal metastasis. The findings showed that the revised Tokuhashi score may be not an accurate tool for predicting the prognostic survival in Chinese patients with spinal metastasis. The establishment of new scores should be considered based on the effect of modern therapeutic modalities to further improve the survival of spinal metastasis cases in future studies.

## References

- [1] Aaron AD: The management of cancer metastatic to bone. *Jama* 1994, 272(15):1206-1209.
- [2] Arrigo RT, Kalanithi P, Cheng I, Alamin T, Carragee EJ, Mindea SA, Park J, Boakye M: Predictors of survival after surgical treatment of spinal metastasis. *Neurosurgery* 2011, 68(3):674-681; discussion 681.
- [3] Walsh GL, Gokaslan ZL, McCutcheon IE, Mineo MT, Yasko AW, Swisher SG, Schrupp DS, Nesbitt JC, Putnam JB, Jr., Roth JA: Anterior approaches to the thoracic spine in patients with cancer: indications and results. *The Annals of thoracic surgery* 1997, 64(6):1611-1618.
- [4] Finkelstein JA, Zaveri G, Wai E, Vidmar M, Kreder H, Chow E: A population-based study of surgery for spinal metastases. Survival rates and complications. *The Journal of bone and joint surgery British volume* 2003, 85(7):1045-1050.
- [5] Patil CG, Lad SP, Santarelli J, Boakye M: National inpatient complications and outcomes after surgery for spinal metastasis from 1993-2002. *Cancer* 2007, 110(3):625-630.
- [6] Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A: Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: a cancer journal for clinicians* 2018, 68(6):394-424.
- [7] Siegel RL, Miller KD, Jemal A: Cancer statistics, 2020. *CA: a cancer journal for clinicians* 2020, 70(1):7-30.
- [8] Schaberg J, Gainor BJ: A profile of metastatic carcinoma of the spine. *Spine* 1985, 10(1):19-20.
- [9] Wong DA, Fornasier VL, MacNab I: Spinal metastases: the obvious, the occult, and the impostors. *Spine* 1990, 15(1):1-4.
- [10] Patchell RA, Tibbs PA, Regine WF, Payne R, Saris S, Kryscio RJ, Mohiuddin M, Young B: Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial. *Lancet (London, England)* 2005, 366(9486):643-648.
- [11] Sciubba DM, Petteys RJ, Dekutoski MB, Fisher CG, Fehlings MG, Ondra SL, Rhines LD, Gokaslan ZL: Diagnosis and management of metastatic spine disease. A review. *Journal of neurosurgery Spine* 2010, 13(1):94-108.
- [12] Tokuhashi Y, Matsuzaki H, Toriyama S, Kawano H, Ohsaka S: Scoring system for the preoperative evaluation of metastatic spine tumor prognosis. *Spine* 1990, 15(11):1110-1113.
- [13] Tokuhashi Y, Matsuzaki H, Oda H, Oshima M, Ryu J: A revised scoring system for preoperative evaluation of metastatic spine tumor prognosis. *Spine* 2005, 30(19):2186-2191.
- [14] Tomita K, Kawahara N, Kobayashi T, Yoshida A, Murakami H, Akamaru T: Surgical strategy for spinal metastases. *Spine* 2001, 26(3):298-306.

- [15] Zhou X, Liu S, Huo Z, Yao S, Wang Y, Liu Y: Clinical characteristics and surgical treatment of esophageal cancer spinal metastasis - A single center 10-year retrospective study. *Clinical neurology and neurosurgery* 2020, 197:106071.
- [16] Truong VT, Shedid D, Al-Shakfa F, Hattou L, Shen J, Boubez G, Yuh SJ, Wang Z: Surgical Intervention for Patients With Spinal Metastasis From Lung Cancer: A Retrospective Study of 87 Cases. *Clinical spine surgery* 2020.
- [17] Liu S, Zhou X, Song A, Yao S, Wang M, Niu T, Gao C, Huo Z, Liu Y, Wang Y: A Single-Center, 10-Year Retrospective Study on Surgical Treatment and Prognosis Analysis of Differentiated Thyroid Carcinoma with Spinal Metastasis. *Cancer management and research* 2020, 12:9893-9904.
- [18] Bauer HC, Wedin R: Survival after surgery for spinal and extremity metastases. Prognostication in 241 patients. *Acta orthopaedica Scandinavica* 1995, 66(2):143-146.
- [19] Leithner A, Radl R, Gruber G, Hochegger M, Leithner K, Welkerling H, Rehak P, Windhager R: Predictive value of seven preoperative prognostic scoring systems for spinal metastases. *European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society* 2008, 17(11):1488-1495.
- [20] Zhang D, Xu W, Liu T, Yin H, Yang X, Wu Z, Xiao J: Surgery and prognostic factors of patients with epidural spinal cord compression caused by hepatocellular carcinoma metastases: retrospective study of 36 patients in a single center. *Spine* 2013, 38(17):E1090-1095.
- [21] Quraishi NA, Manoharan SR, Arealis G, Khurana A, Elsayed S, Edwards KL, Boszczyk BM: Accuracy of the revised Tokuhashi score in predicting survival in patients with metastatic spinal cord compression (MSCC). *European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society* 2013, 22 Suppl 1(Suppl 1):S21-26.
- [22] Horn L, Sandler A: Epidermal growth factor receptor inhibitors and antiangiogenic agents for the treatment of non-small cell lung cancer. *Clinical cancer research : an official journal of the American Association for Cancer Research* 2009, 15(16):5040-5048.