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Accuracy of Revised Tokuhashi Scoring System and Prognostic Factors to Predict Life Expectancy in Lung Cancer Patients with Spinal Metastasis

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Purpose: This study aimed to verify the accuracy of the revised Tokuhashi scoring system to identify the prognosis and life expectancy of lung cancer patients with spinal metastasis. We also aimed to find the factors that were related to the prognosis and actual death.

Method: Lung cancer patients with spinal metastasis who were diagnosed between January 2014 to December 2018 were included in this study. Demographic data, radiographic data, revised Tokuhashi score parameters, actual death, and treatment administered were collected from the hospital tumor database. The relationship between each parameter and actual death were collected and multivariable logistic regression analysis was used to explore the associated factors.

Results: Totally 181 patients were included in this study. The accuracy of the revised Tokuhashi scoring system in this study was 80.68% for scores 0-8 and 100% for scores ≥ 9. Sensitivity and specificity were 100%and 80.7%, respectively, for the prediction of life expectancy ≥ 6 months. LR+ was 5.18. Female (HR=0.58, *P*=0.001), good general condition (HR=0.34, *P*=0.036), none of extra spinal foci metastasis (HR=0.40, *P*=0.002), 1 or 2 extra spinal foci metastasis (HR=0.54, *P*=0.003), radiation (HR=0.57, *P*=0.02), and chemotherapy (HR=0.51, *P*=0.004) were the associated factors with statistical significance.

Conclusion: The revised Tokuhashi scoring system for lung cancer with spinal metastasis had satisfactory accuracy rate to predict life expectancy, especially for > 6 months (score ≥ 9). We also found that females, good general condition, number of extra spinal foci < 3, radiation, and chemotherapy were significantly good prognoses for life expectancy.

Keywords: neoplasm, lung cancer, spinal metastasis, prognosis, life expectancy, scoring system

In recent years, lung cancer has been a leading cause of death worldwide and continues to be on a rise[1,2]. Lung cancer is also the most common cancer in the Thai population according to the National Cancer Institute in Thailand. In the hospital population, we found that lung cancer accounts for 22 % of all the cancer deaths between 2014 to 2018. Lung cancer not only has a high mortality rate, but also can lead to suffering, poor quality of life, and disability owing to spinal metastasis.

The prognosis of metastatic spine tumors remains an essential element. Prognosis refers to the result of a disease and the chance of recovery. It

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may vary according to functional score, histologic type, stage of the tumor, and metastasis. Prognosis not only helps cancer patients and their health care team to decide on a treatment plan but also helps them to know their life expectancy[3-10].

Among people with metastatic spinal tumors, we use a scoring system to predict the prognosis and life expectancy. One of the most popular scoring systems is the revised Tokuhashi scoring system which identifies the prognosis and life expectancy. These scoring systems focus on primary cancer, general condition of the patient, extraspinal bone metastases, vertebral metastases, internal organ metastases, and neurological examination[9-14].

Nowadays, advancements in medical technology have allowed us to investigate and treat lung cancer more efficiently resulting in a longer life expectancy of this disease. However, there are certain limitations in this scoring system that need to be acknowledged; especially the limited accuracy in predicting morbidity of patients who have a life expectancy of more than 1 year.

In this study, we aimed to verify the accuracy of the revised Tokuhashi scoring system to identify the prognosis and life expectancy of metastatic spine tumor patients. We also aimed to find the factors that were related to prognosis and actual death.

MATERIALS AND METHODS

A retrospective cohort study was conducted. The inclusion criteria were: lung cancer patients with spinal metastasis, who were diagnosed and treated between 2014 to 2018. The exclusion criteria included patients with incomeplete documents, lack of imaging data, lost to follow-up and those diagnosed from other hospitals.

Patients' data were collected from the tumor registry of the hospital. We collected the revised Tokuhashi score parameters and other factors for predicting life expectancy which comprises age, gender, level of metastasis, general condition, number of extraspinal metastasis foci, number of metastases in a vertebral body, metastasis to other internal organs, primary site of malignancy, palsy, surgery, chemotherapy, and radiation from the hospital database. The general condition was determined based on the Karnofsky Index, which is divided into three groups: Poor (10%–40%), Moderate (50%–70%), and Good (80%–100%). The neurological status was determined by the Frankel score, which was classified into Complete (Frankel A, B), Incomplete (Frankel C, D), and None (Frankel E).

All the data were calculated using the revised Tokuhashi score; then we compared the prognosis from the revised Tokuhashi score and the actual death of patients from the hospital database. Subsequently, the accuracy and associated factors from these data were analyzed.

Statistical analysis

All data were presented as frequencies and percentages, or means and standard deviations, as appropriate. Fisher exact tests were used to test for relationships between categorical variables to examine proportional differences. Two sample t-tests were performed to examine mean differences between groups. To assess the associated factors of the actual death, we performed univariable and multivariable cox-proportional hazard model analyses. All statistical analyses were conducted using STATA software (version 14.0) for Mac (StataCorp, College Station, TX, USA). Statistical significance was set at p-value < 0.05.

RESULTS

Demographic data

In this study,181 patients were included. The demographic data of the patients are presented in Table 1. We found that the mean age of the patients was 64.19±11.08 years, and 60 (59.67%) patients were male. According to the revised Tokuhashi scoring system, each parameter and treatment were recorded. A total of 60.77% of patients had multiple body metastases and combined levels. Patients with thoracic, cervical, lumbar and sacrum levels were 25.41%, 3.31%, 8.84%, and 1.66%, respectively. The severity of paralysis (Frankel classification) was A, B in 4.97%, C, D in 71.27%, and E in 23.76%.

Table 1 Demographic data of the patients.

Demographic data	Total
Age (mean)	64.19 (±11.08)
>65 years	54.7%
Male	59.67%
Level of metastasis	
Single	39.23%
Multiple	60.77%
Level	
Cervical	3.31%
Thoracic	25.41%
Lumbar	8.84%
Sacrum	1.66%
Combined	60.77%
Tokuhashi score (total)	4.64 (±1.74)
0-8	97.24%
9-11	2.76%
12-15	0%
General condition	
Poor	2.76%
Moderate	71.27%
Good	25.97%
No. of extraspinal bone metastases	
≥3	23.20%
1-2	59.12%
0	17.68%
No. of metastases in the vertebral	
≥3	72.38%
2	24.31%
1	3.31%
Metastases to the major internal	
Unremovable	23.76%
Removable	50.28%
No metastasis	25.97%
Neurological status	
Complete (Frankel A, B)	4.97%
Incomplete (Frankel C, D)	71.27%
None (Frankel E)	23.76%
Spinal surgery	1.10%
Radiation therapy	13.26%
Chemotherapy	16.02%
Mean time till death (Months)	4.14 (±4.35)
<6 months	78.45%
6-12 months	16.02%
>12 months	5.52%

After we summarized the revised Tokuhashi score, we found that scores 0-8 group, 9-11 group, and 12-15 group were approximately 97.24%, 2.76%, and 0%, respectively. We found that the patients who performed spinal surgery were only 1.10%, whereas 13.26% and 16.02% underwent radiation therapy and chemotherapy, respectively.

The mean time till death was 4.14 (±4.35) months. Out of the 118 patients, 78.45% patients deceased within 6 months, 16.02% patients deceased between 6-12 months and 5.52% patients had a life expectancy of more than 12 months. Kaplan-Meier survival estimate curve for lung cancer patients with spinal metastasis is depicted in Fig. 1 and Fig. 2.

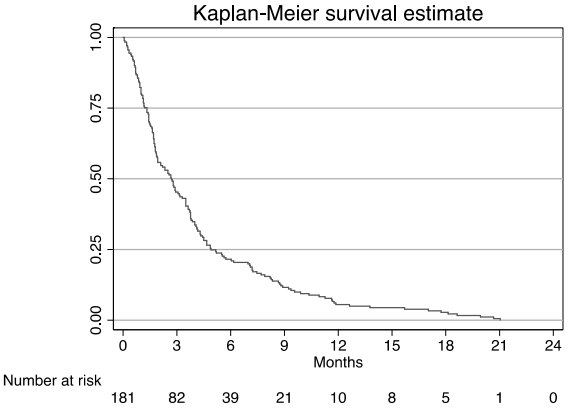

Fig. 1. Kaplan-Meier survival estimate curve for lung cancer patients with spinal metastasis.

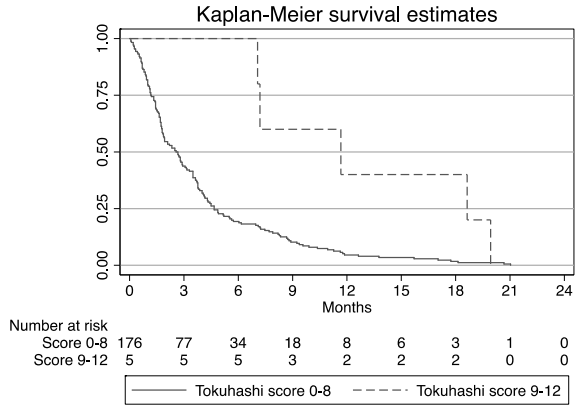

Fig. 2. Kaplan-Meier survival estimate curve for lung cancer patients with spinal metastasis compared between Tokuhashi scores 0-8 and 9-12.

Univariable cox-proportional hazard model analysis (Table 2)

After we collected all the parameters, we used a cox-proportional hazard model analysis. We found that Tokuhashi score (point 9-12, HR 0.32, *P*=0.012), general condition (good general condition, HR 0.33, *P*=0.02), number of extraspinal foci (None of the extraspinal foci, HR 0.41, *P*<0.001), number of metastases in the vertebral body (two

vertebral bodies, HR 0.66, *P*=0.019), metastasis to the major internal organs (No metastasis, HR 0.38, *P*<0.001), neurological status (Frankel E, HR 0.40, *P*=0.015) and chemotherapy (HR 0.50, P=0.001) were significantly associated with life expectancy as protective factors. However, there were no significant differences in age, sex, level of metastasis, spinal surgery, and radiation therapy in this group (*P*>0.05).

Table 2 Univariable cox-proportional hazard model analysis of prognosis factors in lung cancer patients with spinal metastasis.

Risk	HR	*P*-value
Age > 65 y	0.98 (0.74-1.32)	0.928
Sex		
Female	0.66 (0.49-0.90)	0.008
Level of metastasis		
Single	Ref	
Multiple	1.12 (0.83-1.51)	0.476
Level		
Cervical	Ref	
Thoracic	1.27 (0.54-2.98)	0.582
Lumbar	0.99 (0.39-2.54)	0.982
Sacrum	1.16 (0.29-4.67)	0.465
Combine	1.30 (0.57-2.96)	0.535
Tokuhashi score		
0-8	Ref	
9-12	0.32 (0.13-0.78)	0.012
General condition		
Poor	Ref	
Moderate	0.56 (0.23-1.38)	0.212
Good	0.33 (0.13-0.84)	0.020
No. of extraspinal bone		
≥3	Ref	
1-2	0.73 (0.51-1.05)	0.088
0	0.41 (0.25-0.68)	<0.001
No. of metastases in the		
≥3	Ref	
2	0.66 (0.46-0.93)	0.019
1	0.66 (0.29-1.50)	0.324
Metastases to the major		
Unremovable	Ref	
Removable	0.81 (0.56-1.16)	0.252
No metastasis	0.39 (0.25-0.60)	<0.001
Palsy		
Complete (Frankel A, B)	Ref	
Incomplete (Frankel C, D)	0.86 (0.44-1.71)	0.674
None (Frankel E)	0.40 (0.19-0.83)	0.015
Spinal surgery	0.16 (0.21-1.14)	0.067
Radiation therapy	0.68 (0.44-1.05)	0.084
Chemotherapy	0.50 (0.33-0.76)	0.001

Multivariable cox-proportional hazard model analysis (Table 3)

After multivariable cox-proportional hazard model analysis, we found that female gender (*P*=0.001), general condition (good general condition *P*=0.036), number of extraspinal foci (1-2 foci, *P*=0.003, none of extraspinal foci, *P*=0.002), radiation (*P*=0.02), and chemotherapy (*P*=0.004) were significantly associated with life expectancy.

However, there were no significant differences in age, number of metastases in the vertebral body, metastases to the major internal organs, palsy, spinal surgery in this group (*P*>0.05).

Table 3 Multivariable cox-proportional hazard model analysis of prognosis factors in lung cancer patients with spinal metastasis.

Risk	HR	*P*-value
Age > 65 y	1.00 (0.98-1.01)	0.532
Sex		
Female	0.58 (0.42-0.80)	0.001
General condition		
Poor	Ref	
Moderate	0.49 (0.19-1.27)	0.143
Good	0.34 (0.13-0.93)	0.036
No. of extraspinal bone		
≥3	Ref	
1-2	0.54 (0.37-0.81)	0.003
0	0.40 (0.22-0.72)	0.002
No. of metastases in the		
≥3	Ref	
2	0.78 (0.53-1.16)	0.225
1	0.83 (0.35-1.95)	0.669
Metastases to the major		
Unremovable	Ref	
Removable	0.75 (0.50-1.13)	0.259
No metastasis	0.66 (0.39-1.11)	0.120
Palsy		
Complete (Frankel A, B)	Ref	
Incomplete (Frankel C, D)	1.04 (0.51-2.13)	0.911
None (Frankel E)	0.72 (0.32-1.63)	0.430
Spinal surgery	0.77 (0.09-6.70)	0.816
Radiation therapy	0.57 (0.35-0.92)	0.020
Chemotherapy	0.51 (0.32-0.80)	0.004

Score Accuracy

We collected the data of actual death and each parameter of the revised Tokuhashi score, and subsequently summarized the score. We created a 2 by 2 table (Table 4) between the revised Tokuhashi

score (0-8= 176 patients, 9-15= 5 patients) and actual death (< 6 months, ≥ 6 months) for the calculated statistical value.

Table 4 Total score and actual death.

Tokuhashi score	Death predicted	Actual death < 6 months	Actual death ≥ 6 months	Accuracy for prediction
0-8	< 6 mo.	142	34	80.68%
9-15	≥ 6 mo.	0	5	100%

From the study, we found that the accuracy of the revised Tokuhashi scoring system for this population was 80.68% (74.93% – 86.43%) for revised Tokuhashi score 0-8 (176 patients) and 100% for revised Tokuhashi score 9-11 (5 patients).

As presented in Table 4, the sensitivity and specificity were 100% (95% CI=47.8 – 100) and 80.7% (74.1 – 86.2), respectively, for the prediction of life expectancy ≥ 6 months. The positive predictive value was 12.8% (95% CI=4.3 – 27.4) and the negative predictive value was 100% (95% CI=97.4 – 100). The positive likelihood ratio was 5.18 (95% CI=3.83 – 7.0).

DISCUSSION

The life expectancy of metastatic spinal tumor patients associated with lung cancer has been dependent on primary tumor biology, number of metastases, and neurological deficit. Lung cancer patients with spinal metastasis typically have restricted life expectancy[15]. However, the advancements in medical technology prolongs the life expectancy of these patients. In this study, we aimed to find the accuracy of the revised Tokuhashi scoring system for identifying the prognosis and life expectancy of metastatic spinal tumor patients. Several studies have previously reported the accuracy of the revised Tokuhashi score to predict life expectancy. However, the accuracy of each study varies based on different populations and primary sites of malignancy.

From the original study, Tokuhashi et al.[9] found that the rate of consistency between the prognosis score and actual survival period was approximately 86.4% in the prospective study and 82.5% in the retrospective study. Meanwhile, Quraishi et al.[10] studied 233 patients by dividing them into three groups and found that the total accuracy for all the three groups were only 66% (64% for scores 0-8, 64% for scores 9-11, 69% for 12-15). Yeung Yuk-Nam et al.[14] had studied 128 southern Chinese patients and reported that the accuracy was 79%. In the score 0-8 group, they found that the accuracy was 84%; whereas, in the 9-12 and 12-15 groups, the accuracy was 69% and 63%, respectively.

In this study, most of our patients' scores of < 9 point due to lung cancer was assigned 0 point in the primary site category (the total achievable score was 10). The revised Tokuhashi score of ≥ 9 points had a hazard ratio 0.32 (P=0.012) which is a significantly good prognostic factor. The accuracy of the revised Tokuhashi scoring system for scores 0-8 group was 80.68 %, and scores ≥ 9 group were 100%, in this study. Sensitivity was 100% (95% CI=47.8–100) and the positive likelihood ratio was 5.18 (95% CI=3.83–7.0) which means that the revised Tokuhashi scoring system satisfactorily predicted the prognosis and helped to choose the proper treatment, especially for the patients, who had life expectancy > 6 months.

Previous studies had reported that female, non-smoking, non-cervical level, no extraspinal bone metastasis, no visceral metastasis, no pathological fracture, normal neurological examination, and good general condition were good prognosis factors[15-20]. For multivariable analysis in our study, female, good general condition, and number of extraspinal bone metastases less than three sites were good prognostic factors with statistical significance, related to life expectancy. Neurological status was not statistically significant in this study. However, owing to the aggressive nature of lung cancer, a neurological status that affects ambulatory status might not affect the life expectancy of patients. Chemotherapy and radiation affected the survival of patients[21], which were good prognostic factors. However, surgical treatment was not statistically significant in life expectancy but improved the functional outcome of patients[21,22], similar to our study result. According to the results, treatment options for these patients should be discussed, and risk-benefit should be

considered. We preferred chemotherapy and radiation to surgical treatment in lung cancer patients with spinal metastasis.

There were several limitations in this study. First, some patients delayed treatment and investigation owing to financial problems, lack of health awareness, and lost to follow-up. Thus, the accuracy and prognosis of the score in this study may vary from the score of the other population. Second, our patients did not survive more than 12 months which limited the information for those groups. Third, this study had inadequate documenttation of medical records, incomplete imaging, and no diversity of treatment; therefore some patients had to be excluded from this study. This might affect the statistical power of the study. Despite these limitations, this study focused on only lung cancer which was the strength of this study.

A well-designed prospective study should be conducted to gain further insight of parameters and scoring system that predict life expectancy of lung cancer with spinal metastasis patients

CONCLUSION

For lung cancer, the accuracy of the revised Tokuhashi scoring system in this study was 80.68% for scores 0-8 and 100% for scores ≥ 9 points. We also found that the gender, general condition, number of extra spinal foci, radiation, and chemotherapy were significantly associated with life expectancy. These parameters should be considered for appropriate treatment selection and prognosis discussion with the patients.

Disclosure and Conflicts of interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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