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Analysis of Four Scoring Systems for the Prognosis of Patients with Metastasis of the Vertebral Column

Péter Pollner PhD. (3) */divided 1st author/*, Anna Horváth MD., PhD (4) */divided 1st author/*, Tamás Mezei (2), Péter Banczerowski MD., PhD. (1, 2) Gábor Czigléczki MD. (1, 2)

1: National Institute of Clinical Neurosciences, Budapest, Hungary

2: Department of Neurosurgery, Semmelweis University, Budapest, Hungary

3: MTA-ELTE Statistical and Biological Physics Research Group

4: 3rd Department of Internal Medicine, Semmelweis University, Budapest, Hungary

Corresponding author:

Gábor Czigléczki MD

National Institute of Clinical Neurosciences, Hungary, Budapest

1145, Amerikai út 57.

Phone: +36 1 467 9300

Email: gczigleczki@gmail.com

Key words

spinal metastases, prognostic factors, prognosis scoring systems,

Abbreviations and Acronyms

CI: Confidence Interval

CR: Consistency rate

KM: Kaplan-Meier

OS: Overall survival

Abstract

OBJECTIVE: Metastatic spinal diseases are common health problems and there is no consensus on the appropriate treatment of metastases in several conditions. Using clinical measures (e.g., survival time and functional status), prognosis prediction systems advise on the appropriate interventions. The aim of this article is to assess and compare 4 widely used scoring systems (revised Tokuhashi, Tomita, van der Linden, and modified Bauer scores) on a single-center cohort.

METHODS: A retrospective study was designed of 329 patients who were subjected to surgery because of meta-static spinal diseases. Subpopulations according to the classifications of the 4 scoring systems were identified. The overall survival was calculated with the Kaplan-Meier formula. The difference between the survival curves of subpopulations was analyzed with log-rank tests. The consistency rates for the 4 scoring systems are calculated as well.

RESULTS: The follow-up period was 8 years. The median survival time was 222 days. The overall survival of prognostic categories in 3 scoring systems was significantly different from each other, but we found no differences between the categories of the van der Linden system. In this cohort, the revised Tokuhashi system gave the best approximation for survival, with a mean predictive capability 60.5%.

CONCLUSIONS: The evaluation of 4 standard scoring systems showed that 3 were self-consistent, although none of systems was able to predict the survival in our cohort. Based on the predictive capability, the revised Tokuhashi system may provide the best predictions with careful examination of individual cases.

Introduction

The vertebral column is the third most common site for metastasis after pulmonary and hepatic secondary lesions and the most common site for skeletal lesions. [1,2] It affects 7% of patients with oncologic diseases. [3] Symptoms caused by tumors could be pain or motoric or sensory deficits caused by spinal cord or nerve root compression. [4-7] Optimal treatment should take into account the patient's general condition and life expectancy. Patients expected to have long survival benefit from invasive surgical treatment or from high-dosage radiation therapy or from a combination of these 2 treatments. In contrast, patients expected to have shorter survival because of their poor general condition may benefit from more conservative solutions (low-dosage radiation therapy, palliative or minimally invasive surgical options, or supportive care). [4,8-10]

To make evidence-based choices for optimal care, several prognosis predicting systems have been created for treatment of metastatic spinal tumors. [11] These systems combine risk factors with different weights and classify patients into different prognostic groups. For each prognosis category, a treatment is proposed based on the predicted survival. The aim of this article is to analyze 4 prognostic scoring systems of patients with spinal metastasis. These scoring systems are used in spinal neurosurgical practice to determine the best treatment choices in these oncologic cases.

Methods

Patient database and examined prognostic systems

The patient cohort for the analysis was compiled from the electronic medical record at the National Institute of Clinical Neuroscience, in Budapest, Hungary. We identified 382 operations in 337 patients who underwent surgery because of vertebral metastasis, and we had information about the date of last surgery for 329 patients. The operations were performed from December 2007 to December 2015. The status of the patient or the date of death was

checked in December 2016. The only inclusion criterion was a positive diagnosis with metastatic spinal lesions and surgical treatment of the lesions. Some of the patients (n 1⁄4 38) had more than 1 surgical intervention (31 patients with 2 interventions and 7 patients with 3 interventions; none of the patients had >3 interventions).

The 4 examined scoring systems were the following:

- Tokuhashi et al. [12-16] reported a scoring system in 1989, and after 16 years, in 2005, the same group reported a revised version **(Table 1).**
- The system by Tomita and Kawahara [17] was constructed from a retrospective analysis in 2001 **(Table 2)**
- Bauer et al[18]. reported their system in 1995. Later, Leithner et al. [19] and Wibmer et al. [20] modified the Bauer score, omitting the pathologic fractures as a risk factor, and they reported better prediction values **(Table 3)**
- The scoring system by van der Linden et al. [21] was reported in 2005 **(Table 4)**

We collected all data to score patients by these systems. Demographic and baseline clinical variables of interest included sex and age at time of surgery. Baseline functional status was measured by Karnofsky Performance Status. Further data about the status of the patient was recorded such as main clinical symptoms, presence of motoric or sensory deficit, Frankel scores, extraspinal bony metastases, and metastases in the internal organs. About the surgical intervention, we extracted the following factors: affected vertebral levels, steps of intervention, postoperative condition, and the length of hospital stay. Each patient history consisted of data about the metastasis (categorized by primary site of origin), histologic diagnoses, and other comorbidities.

Statistical analysis

Survival was calculated from the date of the last operation and either from the date of death or from the latest follow-up. In cases of death, we had access only to the date, and the cause of death was not registered in our database. We created survival curves by using a Kaplan-Meier (KM) formula and compared them with a log-rank test. P values <0.05 were considered significant. We calculated the consistency rates (CRs) between the predicted prognosis and the actual survival in our cohort (1-KM or KM as appropriate) following the definition by Tokuhashi et al. [15] for the evaluation of predicted survival by the scoring system calculated from data of the cohort. Calculations were made by R software version 3.0.2 (R Foundation for Statistical Computing, Vienna, Austria) [22].

Results

Survival and oncologic data of the population

We identified 337 patients, 199 (59.1%) male and 138 (40.9%) female, with a mean age of 63 years (range, 15e88 years). Overall survival (OS) was calculated by the KM formula. Median OS (amount of time when 50% of the patients have died) was 222 days, and the 95% confidence interval (CI) ranged from 175 to 274 days. The prevalence of the most common primary tumors was distributed as follows: lung (n 1⁄4 84, 24.9%), multiple myeloma (n 1⁄4 38, 11.3%), breast (n 1⁄4 30, 8.9%), cancer of unknown primary site (n 1⁄4 30, 8.9%), kidney (n 1⁄4 26, 7.7%), prostate (n 1⁄4 22, 5.6%), and colorectal (n 1⁄4 22, 6.5%). Sixty-six patients had no internal metastasis (19.6%) and 53 had no other skeletal metastasis (15.7%).

Examinations of the prognosis systems

Revised Tokuhashi score

Because in the revised Tokuhashi score (Table 1), many tumor types with different malignancies and prognosis form a group (2 points, “other” category), we had to categorize our patients with different primary tumor types. We sscored the patients according to histologic similarities and oncologic treatment possibilities (Table 5). We also used this method for the Tomita system (Table 6). The modified Bauer and van der Linden scores did not need any modification because they are accurate about which types of tumors receive points and they do not provide examples. We compared the survival of groups of patients in the 3 prognostic categories. We found that these categories are significantly different according to survival; the log-rank test reported $P < 0.001$. We tested each category to check the deviation from the other 2 categories. Each category was found to be different, but with various P values: conservative group (0-8 points), $P < 0.001$; palliative group (9-11 points), $P<0.001$; and excisional group (12-15 points), $P = 0.013$ (Figure 1). We calculated the CRs for each prognostic category as well (Table 7). The most accurate prediction was observed in the palliative category, in which the system predicted with 95% CI the real OS time with 57% to 74% probability. On average, the system predicted with an accuracy of 60.5% in our cohort.

Tomita score

We also had to make some specifications to the classification of Tomita primary tumor categories (Table 2). Our extended scoring method of Tomita primary tumor categories is

shown in Table 6, which is categorized by histologic similarities and oncologic treatment possibilities. The prognostic categories were significantly different according to survival ($P < 0.001$). We tested all 4 categories separately as well, to establish whether they were different from the rest of the population. All were significantly different: long-term (2e3 points), $P < 0.001$; midterm (4e5 points), P 1⁄4 0.007; short-term (6e7 points), $P < 0.001$; and terminal (8e10 points), P 1⁄4 0.008. The KM curves are shown in Figure 2. Next, we examined the accuracy of the predicted survival (Table 8). The CRs in the last column of Table 8 show that there is a serious difference between our findings and the predicted survival of the Tomita system. For this cohort, the OS was predicted correctly by this system with an average accuracy of only 28.8% of the patients, calculated as the average of the last column of Table 8.

Modified Bauer score

This scoring system separated the cohort into significantly different groups ($P < 0.001$) according to OS. Each group was different from the rest of the population as well: the short survival group (0-1 point), $P = 0.0013$; moderate survival group (2 points), $P < 0.001$; and long survival group (3-4 points), $P < 0.001$ (see Figure 3 for KM curves). The predictive value of this system is shown in Table 9. This system could not be regarded as accurate (29.5% of global prediction ability), especially for the moderate group, which resulted in a low CR. OS was predicted correctly for only 6.3% of the patients with a modified Bauer score of 2.

Van der Linden score

This system was the only one in which the prognostic groups were not significantly different (Figure 4). We examined the prediction ability of this system as well (Table 10). Although the van der Linden system did not separate groups of patients with significantly different KM curves, its average prediction ability (48.6%) is better than that of the modified Bauer and Tomita values.

Discussion

Scoring systems were introduced in neurosurgical practice to determine the best treatment decisions in metastatic spinal diseases. The aim of our study was to compare 4 well-known systems and analyze them to identify which presents the best prediction results.

The revised Tokuhashi scoring system [15] (Table 1) is widely used in clinical practice and receives much attention. In a restricted cohort of patients with only hepatocellular carcinoma, Chen et al. [23] also compared the predictive ability of the 4 scoring systems. The main result of their study agrees with that of the present analysis: the revised Tokuhashi system has the best ability to predict survival (Figure 1). However, there are notable variances among the exact performances of the revised Tokuhashi scores in the literature. When Tokuhashi et al. [16] investigated the ability of their system, they found an 88% predictive probability, Yamashita et al. [24] reported 79%, and Hessler et al. [25] reported 67%, when the calculations were based on cohorts of <100 patients. Eap at al. [26] reported the reproducibility and usefulness of the system in a 260-patient population and found a weighted Cohen k coefficient of 0.41 (95% CI, 0.33-0.50). Our results confirm the findings in the literature. For the conservative category, the survival for 62% of the patients matched the prediction of the system, for the palliative category, this value was 65%, and for the excisional group, it was 54%. On average, the system has 60.8% predicting ability. This value is near the mean in the literature (i.e., 66%).[27-29] We found also that the scoring system separates the groups of patients with different prognosis with a very strong significance, and the conservative category was most significantly separated from the rest of the population (Table 7).

Bauer et al. [30] showed that the Tomita scoring system (Table 2) separates patients into groups with good and bad prognosis. We found similar results by showing that the survival curves of the categories of the Tomita system are significantly different from each other (Figure 2). The most separated group was the one with patients with long-term prognosis (Table 8). According to our calculations, the Tomita system predicted the survival of patients in our cohort with a low probability (28.8%). The analysis of the modified Bauer score 18 (Table 3) also affirms the findings in the literature. The prognostic groups of this system were significantly different (Figure 3) and 2 groups (the good and the moderate) were significantly different from the rest of the population (Table 9). We calculated the predictive ability of the Bauer system as well and found a low value (29.5%).

van der Linden et al. [21] examined their own van der Linden system (Table 4) and reported a 73% predictive probability. In the cohort in our study, the van der Linden score did not achieve such high results (48.6%). Furthermore, we did not find significant differences between the survival curves of the groups of this system (Figure 4, Table 10).

The scoring systems have their own errors and pitfalls, [7,11,25,31,32] but they are widely accepted in clinical practice. [7,11,24,26,27,33-36] The results are shown in Table 11. Examination of our population showed that the revised Tokuhashi system performs the best prediction results and the results of other prognostic systems (Tomita system and modified Bauer system but not the van der Linden score) are also in accordance with previously reported findings. However, this study is limited by its retrospective design and usually there are large variations in intervention responses because of unrecorded genetic, habitual, and personal features of patients that can modify the results; therefore, the conclusion and consequences must be cautiously considered. To the best of our knowledge, there are no any bigger single-center studies in the literature, so we hope that our research will contribute to knowledge about prognosis predicting scoring systems.

Conclusion

The aim of this article was to analyze 4 prognostic scoring systems of patients with spinal metastasis and determine which presents the best prediction results.

According to our findings, the Tomita and Bauer scores separated the classes of patients with good and moderate prognosis, and patients with poor condition were easily identified with the revised Tokuhashi scoring system. Concerning the ability of predicting average survival, the revised Tokuhashi system was the most reliable. However, we found considerable differences between the predictive values of the scoring systems compared with results in the literature.

Spinal metastatic diseases remain a serious and challenging surgical problem, but early diagnosis and sufficient treatment may prevent serious complications and allow longer survival. Using reliable prognostic scoring systems, the surgical decision can be determined more precisely. We believe that our results could be a possible base for multicentric prospective study in the future to determine the best treatment protocol for patients with spinal metastases.

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Tables

Table 1. The Revised Tokuhashi Score

Predictive Factors	Point(s)
General condition (Karnofsky Performance Status, %)	
Poor (10-40)	0
Moderate (50-70)	1
Good (80-100)	2
Number of extraspinal bone foci	
>=3	0
1-2	1
0	2
Number of metastases in the vertebral body	
>=3	0
2	1
1	2
Metastasis to the major internal organs	
Nonremovable	0
Removable	1
No metastasis	2
Primary site of the cancer	
Lung, osteosarcoma, stomach, bladder, esophagus, pancreas	0
Liver, gallbladder, unidentified	1
Others	2
Kidney, uterus	3

Predictive Factors	Point(s)
Rectum	4
Thyroid, breast, prostate, arcinoid	5
Palsy	
Frankel A, B (complete)	0
Frankel C, D (incomplete)	1
Frankel E (none)	2
Prognostic Categories (Points)	Interpretation
0-8	85% lives <6 months --> conservative treatment or palliative surgery
9-11	73% lives >6 months (and 30% >1 year)--> palliative surgery or (exceptionally) excisional surgery
12-15	95% lives >1 year --> excisional surgery

Table 2 The Tomita Score

Predictive Factors	Point(s)
Primary tumor	
Slow growth (e.g., breast, prostate, thyroid)	1
Moderate growth (e.g., kidney, uterus)	2
Rapid growth (e.g., lung, liver, stomach, colon, primary unknown)	4
Primary tumor	
No visceral metastasis	0
Treatable	2
Untreatable	4
Bone metastasis (including spine)	
Solitary/isolated	1
Multiple	2
Prognostic Categories (Points)	Interpretation
2-3	Long-term local control (mean survival 50 months) --> wide or marginal excision
4-5	Mid-term local control (mean survival 23.5 months) --> marginal or intralesional excision
6-7	Short-term palliation (mean survival 15 months) --> palliative surgery
8-10	Terminal care (mean survival 6 months) --> supportive care, no surgery

Table 3. The Modified Bauer Score

Predictive Factors	Point(s)
No visceral metastasis	1
No lung cancer	1
Primary tumor = breast, kidney, lymphoma, multiple myeloma	1
1 solitary skeletal metastasis	1
Prognostic Categories (Points)	Interpretation
0-1	4.8 monthsesupportive care, no surgery
2	18.2 monthseshort-term palliation, dorsal surgery
3-4	28.4 monthsemid-term local control, dorsoventral surgery

Table 4 The van der Linden Score

Predictive Factors	Point(s)
Karnofsky Performance Status	
80-100	2
50-70	1
20-40	0
Primary tumor	
Breast	3
Prostate	2
Lung	1
Other	0
Visceral metastasis	
No	1
Yes	0
Prognostic Categories (Points)	Interpretation
0-3	4.8 monthseconservative therapy
4-5	13.1 monthsepalliative surgery
6	18.3 monthseexcisional surgery

Table 5. Extended Scoring Method for Revised Tokuhashi Primary Tumor Categories

Points	Primary Site of Cancer (Revised Tokuhashi)
0	Lung, osteosarcoma, chondrosarcoma, stomach, bladder, esophagus, pancreas, angiosarcoma, melanoma, mesothelioma, neuroendocrine carcinoma
1	Liver, gallbladder, unidentified
2	Others, germ cell tumors, other epithelial carcinomas (e.g., tonsils and larynx), hematologic malignancies, parotis
3	Kidney, uterus, cervix, ovarium
4	Colon, rectum
5	Thyroid, breast, prostate, carcinoid tumor, osteoblastoma, chondroma, hemangioma

Table 6. Extended Scoring Method for Tomita Primary Tumor Categories

Points	Primary Tumor (Tomita)
1	Slow growth (e.g., breast, prostate, thyroid, osteoblastoma, chondroma, hemangioma)
2	Moderate growth (e.g., kidney, uterus, cervix, germ cell tumors, other epithelial carcinomas [e.g., tonsils and larynx], hematologic malignancies, parotis)
4	Rapid growth (e.g., lung, liver, stomach, colon, rectum, primary unknown, osteosarcoma, chondrosarcoma, extraskeletal Ewing sarcoma, giant cell bone tumor, angiosarcoma, gallbladder carcinoma, bladder carcinoma, melanoma, mesothelioma, pancreas, neuroendocrine carcinoma, esophagus)

Table 7. Predictive Values of the Revised Tokuhashi System, KM=Kaplan-Meier

Point Category (Points)	Prognosis (days)	Number of Patients	Consistency Rate (1-KM or KM) (95% Confidence Interval)
Conservative (0-8)	<180	138	1-KM: 0.62 (0.529e0.693)
Palliative (9-11)	>180	127	KM: 0.653 (0.575-0.741)
Excisional (12-15)	>365	59	KM: 0.541 (0.422-0.693)

Table 8. Predictive Values of the Tomita System

Point Category	Prognosis (days)	Number of Patients	Consistency Rate (Kaplan-Meier) (95% Confidence Interval)
2-3	>50 x 30	97	0.414 (0.313-0.549)
4-5	>23.5 x 30	105	0.153 (0.093-0.252)
6-7	>15 x 30	84	0.190 (0.120-0.301)
8-10	>6 x 30	41	0.394 (0.266-0.584)

Table 9. Predictive Values of the Modified Bauer System

Point Category	Prognosis (days)	Number of Patients	Consistency Rate (Kaplan-Meier) (95% Confidence Interval)
0-1	>4.8 x 30	26	0.461 (0.305-0.699)
2	>18.2 x 30	108	0.063 (0.029-0.136)
3-4	>28.4 x 30	195	0.363 (0.295e0.446)

Table 10. Predictive Values of the van der Linden System

Point Category	Prognosis (days)	Number of Patients	Consistency Rate (Kaplan-Meier) (95% Confidence Interval)
0-3	>4.8 x 30	263	0.595 (0.539-0.658)
4-5	>13.1 x 30	54	0.407 (0.295-0.562)
6	>18.3 x 30	11	0.455 (0.212-0.973)

Table 11. Evaluation of the Scoring Systems According to the Literature

Reference	Publication Date	Type of Study	Number of Cases/ Number of Articles Identified	Investigated Systems	Conclusion
Zoccali et al. [7]	April 2015	Review	1686/—	Revised Tokuhashi	The mean predicting ability is 63%. It needs critical assessment, especially of patients with 12 months survival
Tokuhashi et al. [11]	July 2014	Review	—/236	Tokuhashi, revised Tokuhashi, Tomita, Bauer, van der Linden, Rades, Katagiri	Effectiveness and pitfalls of all of these systems discussed
Yamashita et al. [24]	May 2011	Prospective	85/—	Revised Tokuhashi	79% of mean predicting ability
Hessler et al. [25]	May 2011	Retrospective	81/—	Revised Tokuhashi	67.1% of mean predicting ability
Eap et al. [26]	March 2015	Retrospective	260/—	Revised Tokuhashi	They confirm the validity of the system
Luksanapruksa et al. [27]	May 2017	Review and meta-analysis	—/3959	Revised Tokuhashi, Tomita, Bauer, van der Linden	Effectiveness and pitfalls of all of these systems discussed

Reference	Publication Date	Type of Study	Number of Cases/ Number of Articles Identified	Investigated Systems	Conclusion
Oliveira et al. [31]	July 2013	Prospective	60/—	Revised Tokuhashi	The system is not useful in guiding treatment
Gakhar et al. [32]	August 2013	Prospective	90/—	Revised Tokuhashi	Only 33.4% of mean survival predictability reported
Papastefanou et al. [33]	2012	Prospective	52/—	Revised Tokuhashi, Tomita	The Tokuhashi score is more valuable than the Tomita score
Wang et al. [34]	April 2012	Prospective	448/—	Tokuhashi and revised Tokuhashi	Both of the systems showed significant predictive value
Aoude et al. [35]	June 2014	Retrospective	128/—	Revised Tokuhashi, Tomita	Both of the systems are useable, but the Tokuhashi system has better accuracy
Petteys et al. [36]	March 2015	Retrospective	30/—	Revised Tokuhashi	The Tokuhashi score can be useful