

Classification and scoring systems for metastatic spine tumors: a literature review

Yasuaki Tokuhashi, Hiroshi Uei and Masashi Oshima

Department of Orthopedic Surgery, Nihon University School of Medicine, Japan

Abstract:

Introduction: Accurate evaluation of metastasis and life prognosis is essential for selecting a suitable therapeutic strategy for metastatic spine tumors owing to limitations in treatment options. For this purpose, various classification, evaluation, and scoring systems have been developed.

Methods: Classification, evaluation, and scoring systems for metastatic spine tumors reported to date were identified by performing a literature search on PubMed. We reviewed the most cited classifications and scorings before 2009, and all classifications and scorings reported after 2010 from the search results.

Results: Six classifications and 23 scorings were reviewed. The classification/evaluation methods are divided into 1) anatomical classification/evaluation methods, 2) evaluation methods for neurological symptoms/instability, and 3) scoring systems for predicting life expectancy. The first 2 were useful for the planning and evaluation of surgical indications. Scoring systems for life prognosis also permitted rough prediction of the outcomes and were useful for the selection of a suitable treatment. However, variation of the patient background, diversity of adopted prognostic factors, and the absence of scoring systems that could predict the outcome with an accuracy of 90% or higher introduced some limitations.

Conclusion: The identified classification, evaluation, and scoring systems have been generally useful for treatment strategies. However, we emphasize the necessity of multidisciplinary development and revision of classification and evaluation methods to adapt to the prolongation of survival associated with increased diversity and improvement of treatment options.

Keywords:

metastatic spine tumor, classification, prognosis evaluation system, treatment modality, surgical indication, decision-making

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Introduction

The objective of treatment for metastatic spine tumors is to improve pain relief and anesthesia and to ensure maximum activities of daily living (ADL) and quality of life (QOL) in the short survival period. Actually, the symptoms and survival periods of patients with metastatic spine tumors vary widely, and sufficient consideration of the severity of symptoms and life prognosis is required for determining an effective therapeutic strategy. Accurate evaluation of metastasis and life prognosis before treatment is the most important factor in determining the therapeutic strategy for metastatic spine tumors.

However, we still lack an absolute evaluation method or prognostic factor. The tumor, lymph nodes, metastasis

(TNM) classification is presently used as an index for primary malignant tumors, and similar indices are used internationally despite some variation among countries. As a result, a rough prognosis has been considered possible using the TNM classification in most cancers.

In spinal metastasis, predicting life expectancy is extremely important for the selection of a suitable therapeutic strategy, and the opinion of the attending physicians treating the primary lesion should be given top priority. However, the life expectancy predicted by them is not necessarily accurate, spinal metastasis itself is diverse, and uniform evaluation is impossible. Therefore, orthopedists and radiologists participating in the treatment have also evaluated spinal metastases and life prognoses from multidisciplinary viewpoints^{1,2)}. In the present study, we reviewed the representative

Corresponding author: Yasuaki Tokuhashi, tokuhashi.yasuaki@nihon-u.ac.jp

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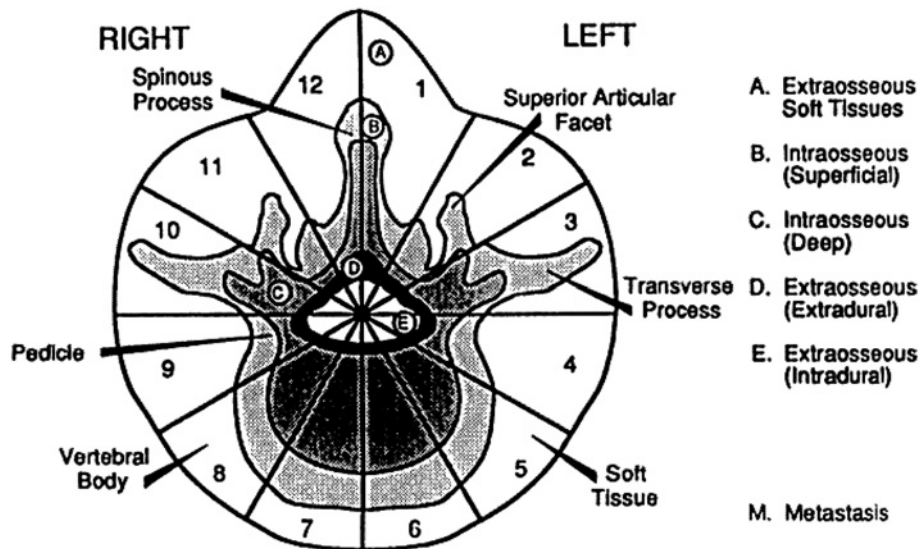


Figure 1. Weinstein, Boriani, Biagini (WBB) classification (1997). This classification presents the vertebral involvement as sections of a clock face (“zones”) centered on the spinal cord, from zone 1 (left spinous process and lamina) through zone 6 (left anterior wedge of vertebral body) and back round to zone 12 (right spinous process and lamina). In addition, the prefixes A-E are used to denote radial levels (“layers”) of vertebral involvement, from extrasosseous paraspinal tissues (A) to extradural (D) and intradural (E) layers (Reproduced from [5] with permission).

classification and scoring systems reported to date.

Methods

A PubMed search was performed using the key words “classification” or “scoring” or “life expectancy” with “metastatic spine tumor” for the years from 1976 to 2016. The search using the keywords “classification” with “metastatic spine tumor” returned 140 articles.

Similarly, the search using the keywords “scoring” returned 67 articles and that using “life expectancy” in combination with metastatic spine tumor”. We reviewed most cited classifications and scorings before 2009, and did recent all classification and scorings which were reported after 2010.

Results

We performed acquisition of documents under former criteria, and reviewed six classifications and twenty-three scorings. Twenty-two of 23 scorings related to prediction of prognosis.

Classification/scoring of metastatic spine tumors: literature review

A. Anatomical classification

Historically, methods of evaluation according to the size and area of involvement of metastatic lesions have been proposed. Classification methods based on the location of the primary spinal tumor have been proposed by Enneking WF et al. (1980)³ and McLain RF and Weinstein JN (1990);⁴ however, they had shortcomings including challenges with

differentiating some categories by images alone and the lack of consideration for spinal cord/nerve compression¹. Boriani S et al. (1997)⁵ proposed a clock type (transverse) classification of tumors according to their location by adding categorization of the dural tube (Fig. 1). This classification method was excellent in that en bloc resection was always intended with preservation of the spinal cord in mind. For this reason, while the classification was useful in surgical planning for primary malignant tumors of the spine, it was not a reasonable method for the classification of spinal metastases, which were treated primarily by palliative decompression and fixation¹.

Tomita K et al. (2001)⁶ proposed a 7-category classification method mentioned above, which evaluated the sagittal involvement of the tumor in the transverse section alone adjusted to metastatic spine tumors (Fig. 2). However, this classification was not necessarily useful, because the intra-compartmental types 1 to 3 are clinically the same category and need not be classified for the selection of treatment¹.

These anatomical classification methods are useful to an extent for the planning of surgery, but they are not necessarily correlated with the life prognosis. In addition, they are not decisive factors for the evaluation of surgical indications¹.

With improvements in magnetic resonance imaging (MRI), it has become easy to evaluate transverse images of the spinal cord, and classification methods aimed to evaluate the severity of spinal cord compression have appeared. Bilsky MH et al. (2010)⁷ classified the degree of compression of the dura mater and spinal cord at the site of maximum compression of the spinal cord by the tumor into 6 grades

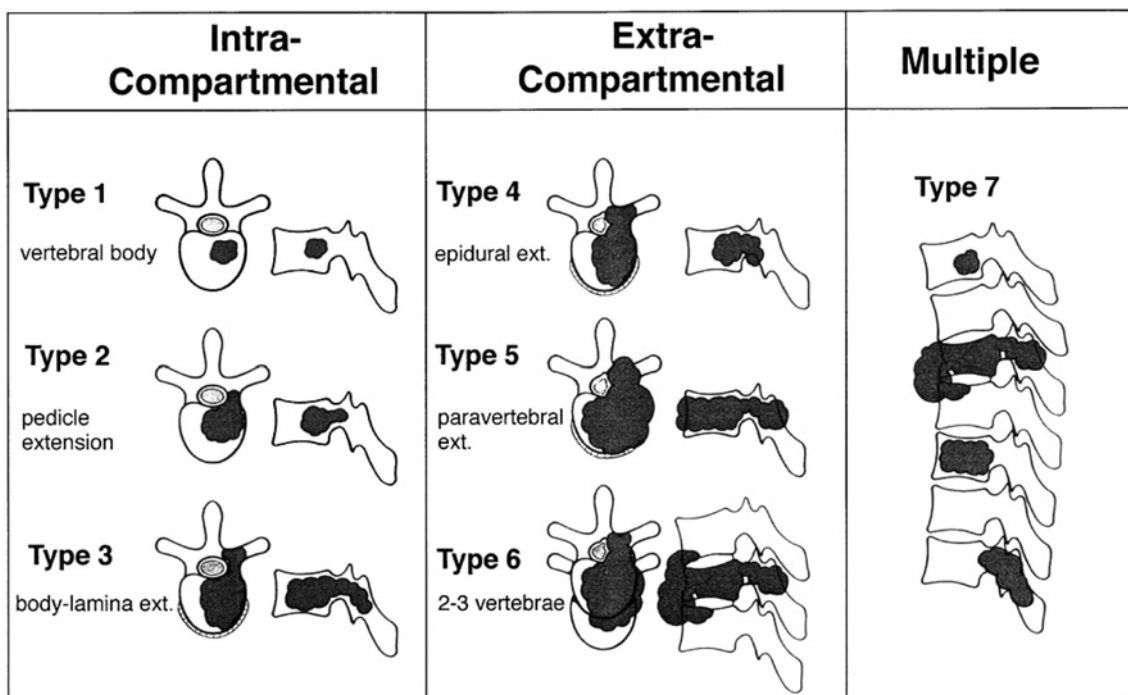


Figure 2. The surgical classification of spinal tumors (2001) (Reproduced from [6] with permission).

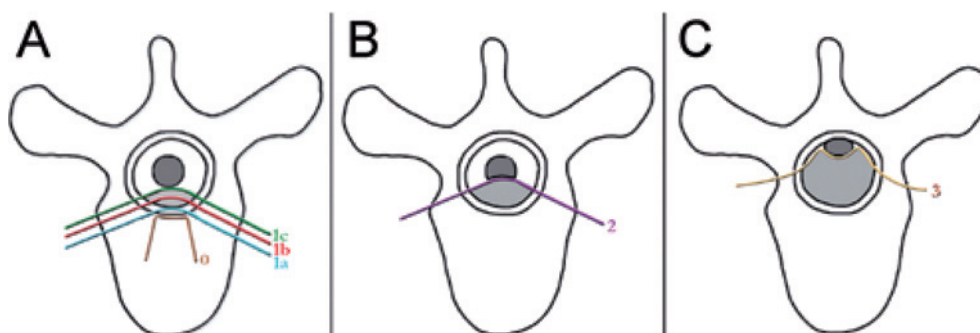


Figure 3. Schematic representation of the 6-point ESCC grading scale (2010). A grade of 0 indicates bone-only disease; that of 1a, epidural impingement, without deformation of the thecal sac; 1b, deformation of the thecal sac, without spinal cord abutment; 1c, deformation of the thecal sac with spinal cord abutment, but without cord compression; 2, spinal cord compression, but with CSF visible around the cord; and 3, spinal cord compression, no CSF visible around the cord (Reproduced from [7] with permission).

according to axial T2-weighted MR images (Fig. 3). They also showed high inter- and intra-observer reliability of this classification. Although the classification has problems, such as the variation of the hardness and progression rate among tumors as well as urgency of spinal cord/nerve paralysis depending on the lesion level of the tumor, replication studies are anticipated, as there have been no classifications concerning spinal cord/nerve compression by tumors.

B. Classification or scoring system for neurological involvement and spinal instability

There are also classification methods based on neurological symptoms and spinal instability rather than the location of tumor. Harrington KD (1986)⁸⁾ proposed a simple 5-grade classification system taking spinal instability and neurologi-

cal symptoms into consideration (Table 1). Because surgery is clearly superior to radiotherapy as a treatment for metastatic spine tumors for the management of spinal instability, this classification method is useful in evaluating surgical indications for spinal metastasis. While it is theoretically excellent, it has limitations in concreteness and objectivity¹⁾. In addition, because of the lack of evaluation of the degree of neurological symptoms, paraplegia and radicular pain are classified in the same category. Therefore, it is difficult to predict life expectancy or functional outcome using this classification¹⁾. To compensate for such a lack of reliability and objectivity, the Spine Instability Neoplastic Score (SINS)⁹⁾ appeared as a new scoring system (Table 2). According to the SINS consisting of 6 categories where the lo-

Table 1. Harrington Classification of Spinal Metastases (1986)⁸⁾.

| | |
|---|---|
| 1 | No neurological involvement |
| 2 | Bone involvement without collapse or instability |
| 3 | Significant neurological impairment without bone involvement |
| 4 | Vertebral collapse with pain or instability, but no neurological impairment |
| 5 | Vertebral collapse with pain or instability and neurological impairment |

Table 2. Spine Instability Neoplastic Score (SINS) Classification According to the Spine Oncology Study Group (SOSG) (2010)⁹⁾.

| | Score |
|---|--------------------|
| Location | |
| Junctional (occipito-C2, C7-T2, T11-L1, L5-S1) | 3 |
| Mobile spine (C3-C6, L2-L4) | 2 |
| Semi-rigid (T3-T10) | 1 |
| Rigid (S2-S5) | 0 |
| Pain* | |
| Yes | 3 |
| Occasional pain but not mechanical | 1 |
| Pain-free lesion | 0 |
| Bone lesion | |
| Lytic | 2 |
| Mixed (lytic/ blastic) | 1 |
| Blastic | 0 |
| Radiographic spinal alignment | |
| Subluxation/ translation present | 4 |
| De novo deformity (kyphosis/ scoliosis) | 2 |
| Normal alignment | 0 |
| Vertebral body collapse | |
| >50% collapse | 3 |
| <50% collapse | 2 |
| No collapse with >50% body involved | 1 |
| None of the above | 0 |
| Posterolateral involvement of spinal elements** | |
| Bilateral | 3 |
| Unilateral | 1 |
| None of the above | 0 |
| Total score | |
| 0-6 | Instability Stable |
| 7-12 | May be stable |
| 13-18 | Unstable |

* Pain involvement with recumbency or pain with movement or loading of the spine.

** Facet, pedicle, or costovertebral joint fracture or replacement with tumor.

cation of spinal metastasis, imaging findings, and pain were combined with a full score of 18, a higher score is considered to indicate more severe spinal instability. Because imaging findings do not necessarily correlate with clinical symptoms, the SINS, incorporating pain as a clinical symptom, is a clinically excellent scoring system. However, it has been reported that images are not easy to evaluate and that

Table 3. Original Tokuhashi Score (1989, 1990)^{11, 12)}.

| Predictive Factor | Score (points) |
|---|---------------------------------|
| General condition (KPS: Karnofsky's performance status) | |
| Poor (KPS 10-40%) | 0 |
| Moderate (KPS 50-70%) | 1 |
| Good (KPS 80-100%) | 2 |
| Number of extraspinal bone metastases foci | |
| ≥3 | 0 |
| 1-2 | 1 |
| 0 | 2 |
| Number of metastases in the vertebral body | |
| ≥3 | 0 |
| 2 | 1 |
| 1 | 2 |
| Metastases to the major internal organs | |
| Unremovable | 0 |
| Removable | 1 |
| No metastases | 2 |
| Primary site of the cancer | |
| Lung, stomach | 0 |
| Kidney, liver, uterus, others, unidentified | 1 |
| Thyroid, prostate, breast, rectum | 2 |
| Spinal cord palsy | |
| Complete | 0 |
| Incomplete | 1 |
| None | 2 |
| Total points | |
| 0-5 | Mean survival periods ≥3 months |
| 6-8 | <12 months |
| 9-12 | ≥12 months |

KPS: Karnofsky performance status¹³⁾

the kappa values of inter- or intra-observer agreement are not necessarily high. Therefore, caution must be exercised in the comparative evaluation of the score among examiners and hospitals¹⁰⁾.

C. Scoring system for predicting life expectancy

1) Classic

Actually, the prognosis of metastatic spine tumor varies widely, and it is a major problem for the selection of treatment. Because general condition exerts a greater effect on prognosis than local condition, the evaluation of disease severity or prediction of outcome was difficult by imaging of the local condition. Therefore, Tokuhashi Y (1989, 1990)^{11,12)} devised a prognostic scoring system consisting of 6 items that are retrospectively considered to affect the outcome (general condition, Karnofsky performance¹³⁾, number of bone metastases other than spine metastases, number of spine metastases, type of the primary lesion, presence or absence of metastasis to major organs, and state of paralysis) (Table 3)^{11,12)}. Statistically, they retrospectively showed that the survival period was correlated with total score in 47 patients and predicted the outcome according to the prognostic criteria based on the total score. In the original version, the expected survival period was 3 months or less when the to-

Table 4. Revised Tokuhashi Score (2005)¹⁴⁾.

| Predictive factor | Score (points) |
|---|---------------------|
| General condition (KPS: Karnofsky's performance status) | |
| Poor (KPS 10-40%) | 0 |
| Moderate (KPS 50-70%) | 1 |
| Good (KPS 80-100%) | 2 |
| Number of extraspinal bone metastases foci | |
| ≥3 | 0 |
| 1-2 | 1 |
| 0 | 2 |
| Number of metastases in the vertebral body | |
| ≥3 | 0 |
| 2 | 1 |
| 1 | 2 |
| Metastases to the major internal organs | |
| Unremovable | 0 |
| Removable | 1 |
| No metastases | 2 |
| Primary site of the cancer | |
| Lung, osteosarcoma, stomach, bladder, esophagus, pancreas | 0 |
| Liver, gallbladder, unidentified | 1 |
| Others | 2 |
| Kidney, uterus | 3 |
| Rectum | 4 |
| Thyroid, prostate, breast, carcinoid tumor | 5 |
| Spinal cord palsy | |
| Complete (Frankel A, B) | 0 |
| Incomplete (Frankel C, D) | 1 |
| None (Frankel E) | 2 |
| Total points | Predicted prognosis |
| 0-8 | <6 months |
| 9-11 | ≥6 months |
| 12-15 | ≥1 year |

KPS: Karnofsky performance status¹³⁾

tal score was 0-5, less than 12 months when the total score was 8 or higher, and 12 months or longer when the total score was 9 or higher. In the revised version of the prognostic criteria, in which primary lesions were scored 0-5 instead of 0-2 (Table 4)¹⁴⁾, the expected survival period was less than 6 months when the total score was 0-8, 6 months or longer when the total score was 9-11, and 1 year or longer when the total score was 12 or higher.

While statistical validation of these scoring systems is insufficient, the factors selected as affecting the survival period were relatively simple and easy to evaluate. In addition, they had no factors of therapeutic intervention, and the criteria were relatively flexible and versatile. Therefore, they have been evaluated by replication studies worldwide including our studies^{15,16)}, and relatively favorable results have been reported^{2,17-19)}.

These papers were the first reports on scoring systems for the prognosis of metastatic spine tumors and have long been landmark articles concerning the prognosis after the revision in 2005¹⁴⁾. Similar scoring systems where factors related to

the outcome are combined have been developed thereafter. In the same period, Yamashita et al. (1990)²⁰⁾ also reported a staging system using bone scintigraphy for the prognosis of spinal metastasis. However, it was not accepted widely as the presence of metastasis to major organs exerted greater effects than the extent of bone metastasis evaluated by bone scintigraphy.

In the revised version of the Tokuhashi score¹⁴⁾, the prognosis was classified into 3 categories with 6 months and 1 year, which are clinically key periods, as cut-off values. While the categorization by this system lacked precision, with the intermediate group partially overlapping the good prognosis group, it was applied inappropriately by rigidly defining scores of 9-11 as corresponding to a survival period of 6 months to 1 year²¹⁻²⁴⁾, and the agreement rate between the prognostic category and survival period was low in all these reports.

In addition, it has been suggested that the agreement rate between the survival period and score differs according to the type of the primary lesion and that the usefulness of the scoring system varies among cancer types. Yamashita T et al. (2011)²⁵⁾ reported that the outcome was consistent with the prognostic category in 67 (79%) of the 85 patients followed-up for 1 year or longer. They also reported that the Tokuhashi score was useful irrespective of the treatment selected. However, while the low total score group showed a high correlation with poor outcome, the outcome was poor for the score concerning the kidney in many patients, and the kidney was suggested to be overweighted in scoring. In the same year, Hessler C et al. (2011)²⁶⁾ maintained that the agreement rate between the revised Tokuhashi score and the actual survival period was 67.1% in a study of 76 patients who underwent surgery for spinal metastasis of lung cancer and that the scoring system was not adapted to recent advancements in the treatment of metastatic spine tumors. Some patients with spinal metastasis of lung cancer survive for 1 year or longer, and the outcome is relatively favorable in patients aged 50 years or less, those with metastasis to the lumbar spine, and those without paralysis. Tokuhashi et al. (2012)²⁷⁾ basically agreed to this contention, admitting that the revised version had been prepared 13 years previously and that some patients with spinal metastases of lung cancer could survive for 2 years or longer as a result of advancements in treatment during this period. However, they refuted that the prognosis of spinal metastasis of lung cancer remained essentially poor and that the precision of the score should be evaluated by including patients for whom only conservative therapy was possible as well as surgically treated patients.

Some studies focused on the degree of differentiation among good prognosis, poor prognosis, and intermediate groups concerning the original and revised Tokuhashi score. Quraishi NA et al. (2013)²⁸⁾ reported that 201 surgically treated patients could be differentiated into poor prognosis, moderate prognosis, and good prognosis groups with the predictive value between the actual and predicted survival of

Table 5. Tomita Score (2001)^{6,32}.

| Prognostic factors | Points |
|--|---------------------|
| Primary tumor | |
| Slow growth (breast, thyroid etc.) | 1 |
| Moderate growth (Kidney, uterus, etc.) | 2 |
| Rapid growth (Lung, stomach, etc.) | 4 |
| Visceral metastases | |
| Treatable | 2 |
| Untreatable | 4 |
| Bone metastases | |
| Solitary or isolated | 1 |
| Multiple | 2 |
| Total points | Predicted prognosis |
| 2-4 | >2 year |
| 4-6 | 1-2 years |
| 6-8 | 6-12 months |
| 8-10 | <3 months |

Table 6. Original Baur Score (1995)⁴².

| Positive prognostic factors | Score (Points) |
|--|--------------------------|
| No visceral metastases | 1 |
| Absence of pathologic fracture | 1 |
| Solitary skeletal metastasis | 1 |
| No lung cancer | 1 |
| Primary tumor=breast, kidney, lymphoma, multiple myeloma | 1 |
| Total score (points) | 1-year survival rate (%) |
| 0-1 | % (<6months survival) |
| 2-3 | 25% |
| 4-5 | 50% |

64% or higher in all groups and 66% in all patients combined and that the scoring system was moderately useful. However, in 142 surgically treated patients reported by Poin-tillart V et al. (2011)²⁹, the agreement rate between outcome and score was 60% or less according to both the original and revised versions.

There have also been studies that compared the original and revised versions. Wang M et al. (2012)³⁰ reported that the revised version of Tokuhashi score was particularly useful for metastases of prostate and breast cancers and that the original version was superior for the classification of metastases of colon cancer. They also observed that both versions were inadequate for metastases of lung and kidney cancers and that the overall precision was higher for the revised version than that for the original version. On the other hand, Liang T et al. (2013)³¹ reported that the original version was more useful than the revised version or Tomita score (2001)^{6,32}.

Tomita et al. (2001)^{6,32} developed a new scoring system by retrospectively reviewing 67 patients including those treated conservatively (Table 5).

Because items constituting the original Tokuhashi score were not differentially weighted, it was revised by weighting each factor of each item using the Cox proportional hazards model. It was simplified by excluding paralysis, which was not considered to affect the life prognosis. In addition, expected survival period and treatment selection including the indication for conservative therapy were specified in detail according to the total score: An expected survival period of 2 years or longer and en bloc excision for scores of 2-4, 1-2 years and debulking for scores of 4-6, 6-12 months and palliative decompression for scores of 6-8, and 3 months or less and terminal care for scores of 8-10.

This scoring system, prepared in a surgical patient-centered manner, is often used for the evaluation of surgical indications along with the Tokuhashi score, and its usefulness has been evaluated in many reports^{2,33-40}.

Baur HCF (2002)⁴¹ considered that this scoring system succeeded in the differentiation between poor and good prognosis groups but suggested underestimation of pain and paralysis, lack of specificity for urgent paralysis, and over-emphasis of aggressive surgical treatments with understatement of indications for conservative therapy and palliative surgery. Baur HCF et al. (1995)⁴² also developed a scoring system based on data from 153 patients with limb bone metastases and 88 patients with spinal involvements. They prepared a simple scoring system by combining 3 items identified as influential by Cox regression analysis after univariate analysis of prognostic factors, i.e., site of primary tumor, metastatic load, and pathological fracture (Table 6). As a result, the 1-year survival rate was 0% in those having scores of 0-1, who all died within 6 months, 25% in those having scores of 2-3, and 50% in those having scores of 4-5. There were several limitations to this scoring system. It was difficult to evaluate the presence or absence of pathological fracture by imaging, and the scoring system was developed based on the data of a multicenter study in surgical cases alone with marked variation in surgical indications and procedures among the facilities.

van der Linden (2005)⁴³ devised a scoring system consisting of 3 items, i.e., Karnofsky performance status, type of the primary lesion (lung cancer, breast cancer, prostate cancer, others), and the presence or absence of metastasis to major organs, based on data from 342 patients with spinal metastases (Table 7) and reported that the system was effective in 73% of the patients⁴⁵.

Comparison of prognostic scoring systems was performed increasingly from around 2008. Leithner A et al. (2008)⁴⁴ and Wibmer C et al. (2011)⁴⁵ reported that, of the 7 scoring systems including the Tokuhashi score, Tomita score, and Linden score; those other than the Bauer scoring system were acceptable until 4 years after treatment. However, the Bauer score and modified Bauer score (Table 8), in which the presence or absence of pathological fracture was excluded, were superior concerning the prognosis after 4 or more years and the differentiation between the good and moderate prognosis groups^{44,45}. According to the modified Bauer scoring system, the median overall survival (OS) was

Table 7. Linden Score (2005)⁴³.

| Prognostic factors | Points |
|------------------------------|-----------------------|
| Karnofsky performance status | |
| 80-100 | 2 |
| 50-70 | 1 |
| 20-40 | 0 |
| Primary tumor | |
| Breast | 3 |
| Prostate | 2 |
| Lung | 1 |
| Other | 0 |
| Visceral metastases | |
| No | 1 |
| Yes | 0 |
| Total points | Mean overall survival |
| 0-3 (n=116) | 4.8 months |
| 4-5 (n=164) | 13.1 months |
| 6 (n=62) | 18.3 months |

Karnofsky performance status¹³

Table 8. Modified Baur Score (2008)^{44, 45}.

| Positive prognostic factors | Points |
|--|-------------------------|
| No visceral metastases | 1 |
| No lung cancer | 1 |
| Primary tumor=breast, kidney, lymphoma, multiple myeloma | 1 |
| One solitary skeletal metastasis | 1 |
| Total points | Median overall survival |
| 0-1 | 4.8 months |
| 2 | 18.2 months |
| 3-4 | 28.4 months |

4.8 months. There was no surgical indication when the score was 0-1, the median OS was 18.3 months and posterior palliative surgery was indicated when the score was 2, and the median OS was 28.4 months and excisional surgery through antero-posterior combined approach was indicated when the score was 3-4. This group further conducted replication studies and reported that the modified Bauer system was superior to the other 6 systems⁴⁶.

Chen H et al. (2010)⁴⁷ reported that the revised Tokuhashi score was practical and the most accurate in prognosis among 4 scoring systems, i.e., the revised Tokuhashi score¹⁴, Tomita score⁶, Bauer score⁴², and revised van der Linden score⁴³, in 41 patients with spinal metastases of hepatocellular carcinoma. Moreover, they proposed the serum albumin and lactate dehydrogenase (LDH) levels as useful prognostic factors.

In addition, in the field of radiology, Rades D et al. (2008)⁴⁸ prepared a few scoring systems retrospectively using data obtained from patients who underwent radiotherapy for spinal cord compression by metastatic tumors. The scoring system was developed from 1,852 cases of spinal metastasis (Table 9)⁴⁸, and they reported the results of its prospec-

Table 9. Rades Score (2008)⁴⁸ and Outcome (2010)⁴⁹.

| Prognostic factor | Score (points) |
|---|------------------|
| Type of primary tumor | |
| Breast cancer | 8 |
| Prostate cancer | 7 |
| Myeloma/lymphoma | 9 |
| Lung cancer | 3 |
| Other tumors | 4 |
| Other bone metastases at the time of RT | |
| Yes | 5 |
| No | 7 |
| Visceral metastases at the time of RT | |
| Yes | 2 |
| No | 8 |
| Interval from tumor diagnosis to MSCC | |
| ≤15 months | 4 |
| >15 months | 7 |
| Ambulatory status before RT | |
| Ambulatory | 7 |
| Nonambulatory | 3 |
| Time of developing motor deficits before RT | |
| 1-7 days | 3 |
| 8-14 days | 6 |
| >14 days | 8 |
| Total score | 6-month survival |
| 20-30 (n=237) | 16% |
| 31-35 (n=162) | 48% |
| 36-46 (n=253) | 81% |

RT, Radiation therapy; MSCC, Metastatic spinal cord compression

tive application to 439 subsequent cases (2010, Table 9)⁴⁹. They also prepared a scoring system for different cancer types. In addition to scoring systems for metastases of prostate cancer (2012)⁵⁰ and metastases of breast cancer (2013)⁵¹, a scoring system for unknown primary tumors has been developed by Douglas et al. (2013)⁵².

In all these scoring systems, conditions for which radiotherapy (RT) is indicated for spinal cord compression in the advanced stage of metastatic tumors are evaluated. Moreover, other bone metastases at the time of RT, visceral metastases at the time of RT, interval from tumor diagnosis to metastatic spinal cord compression (MSCC), ambulatory status before RT, and time of developing motor deficits before RT are selected as factors, and the combination of items and score allocations are modified according to the cancer type. It is important to mention that application of these scoring systems is limited to advanced stages of cancer with spinal metastases and impending paralysis, and that a single pattern is not applied to different cancer types. Because treatment is limited to radiotherapy, scoring systems are not adapted to the recent diversified treatment selections².

The Katagiri score (2005)⁵³ is a scoring system incorporating therapeutic intervention. It was derived retrospectively

Table 10. Katagiri New Score (2014)⁵⁴.

| Prognostic factor | Score |
|---|-------|
| Primary lesion | |
| Slow growth (Hormone-dependent breast and prostate cancer, thyroid cancer, multiple myeloma, and malignant lymphoma) | 0 |
| Moderate growth (Lung cancer treated with molecularly targeted drugs, hormone-independent breast and prostate cancer, renal cell carcinoma, endometrial and ovarian cancer, sarcoma, and others) | 2 |
| Rapid growth (Lung cancer treated without molecularly targeted drugs, colorectal cancer, gastric cancer, pancreatic cancer, head and neck cancer, esophageal cancer, other urological cancers, melanoma, hepatocellular carcinoma, gallbladder cancer, cervical cancer and cancers of unknown origin) | 3 |
| Visceral metastases | |
| Nodular visceral or cerebral metastasis | 1 |
| Disseminated metastases* | 2 |
| Laboratory data | |
| Abnormal** | 1 |
| Critical*** | 2 |
| ECOG PS 3 or 4 | 1 |
| Previous chemotherapy | 1 |
| Multiple skeletal metastases | 1 |

EOG: Eastern Cooperative Oncology Group

* Disseminated metastasis: Pleural, peritoneal, or leptomeningeal dissemination

** Abnormal: CRP ≥0.4 mg/dL, LDH ≥250 IU/L, or serum albumin <3.7 g/dL

*** Critical: platelet <100,000/μL, serum calcium ≥10.3 mg/dL, or total bilirubin ≥1.4 mg/dL

from 350 cases of skeletal metastases and is characterized by the inclusion of chemotherapy history before the onset of spinal metastasis. Initially, the extent of intervention by chemotherapy, individual differences, and sensitivity were evaluated vaguely, and the system had major limitations concerning versatility and objectivity. However, as the survival period of patients has been prolonged recently owing to improvements in adjuvant therapies, such as molecularly targeted drugs, the history of chemotherapy has become an important prognostic factor. Katagiri et al. also reported a new scoring system with modifications of score allocation for breast and prostate cancers according to hormone dependence or independence of the primary lesions and for lung cancer according to the use or non use of molecular targeted drugs and incorporation of laboratory data (Table 10, 2014)⁵⁴. In a series of 808 patients, the 2-year survival rate was reported to be 77.8% in a group with a total score of 0-3, the 1-year survival rate was 49.3%, and the 6-month survival rate was 74.0%, in a group with a total score of 4-6, and the 6-month survival rate was 26.9% in a group with a total score of 7-10.

2) *Significance and problems*

All these prognostic scoring systems were prepared by combining factors that affect the outcome². We found 22 scoring systems by searching the PubMed after the Tokushashi score until 2016^{6,11,12,14,42-45,48-64}. The type of the primary lesion was the only prognostic factor adopted in all these

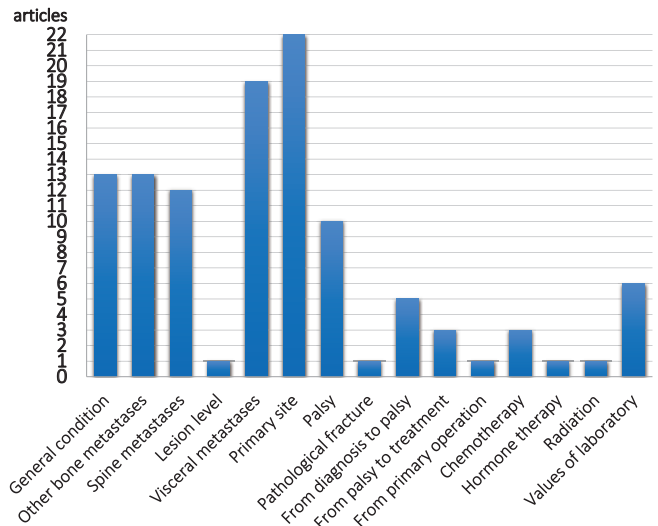


Figure 4. Prognostic factors that were adopted by the 22 scoring systems^{6, 11, 12, 14, 42-45, 48-64}.

scoring systems, and the other factors affecting prognosis were selected differently. Following the type of primary lesion, metastasis to major organs, general condition (performance status), and the number of bone metastases were selected most frequently (Fig. 4).

Rades et al. attached importance to functional factors and reported a scoring system with emphasis on the ambulation ability before treatment and rate of progression of paralysis as prognostic factors^{47-51,54}, but many scoring systems including the one by Tomita completely disregarded paralysis^{6,42-45}. This variation is considered to be explained by the differences in the characteristics of patients evaluated for their preparation. All patients evaluated by Rades et al. had progressive spinal cord paralysis and underwent radiotherapy, and included a considerable number of patients with poor prognoses having no indications for surgery. Therefore, the outcomes of their patients were considerably poorer compared with those of the patients used for the preparation of other scoring systems².

Recent reviews have suggested 1) the function status, 2) number of visceral metastases, and 3) primary tumor pathology as factors that exert the greatest effects on outcome⁶⁵⁻⁶⁷. Moreover, presently, treatment for metastasis is initiated as soon as asymptomatic metastasis is detected. Kawai T et al. (2013) reported that prognostic factors should be reevaluated, because the timing of therapeutic intervention has changed from before⁶⁸. In fact, the occurrence and progression of bone metastasis are suppressed by the administration of bisphosphonates and anti-receptor activator of nuclear factor kappa-B ligand (RANKL) antibody, and it is necessary to evaluate prognostic factors in consideration of the sensitivity to these bone-modifying agents (BMA).

At any rate, such additive scoring systems combining factors that affect the outcome are undoubtedly useful for the general prognosis at present, because there is no single absolute prognostic factor^{2,69}. However, no scoring system has

Table 11. Rades Risk Score for Death within 2 Months after Radiotherapy (2013)⁵⁶.

| Characteristic | Score (points) |
|--|----------------|
| ECOG performance status | |
| 2 | 0 |
| 3-4 | 4 |
| Tumor type | |
| Breast cancer | 1 |
| Prostate cancer | 2 |
| Myeloma/lymphoma | 1 |
| Lung cancer | 3 |
| Other | 3 |
| Further bone metastases | |
| No | 1 |
| Yes | 3 |
| Visceral metastases | |
| No | 1 |
| Yes | 4 |
| Interval from cancer diagnosis to MSCC | |
| ≤15 months | 3 |
| >15 months | 1 |
| Ambulatory status prior to RT | |
| Not ambulatory | 4 |
| Ambulatory before RT | 1 |
| Time of developing motor deficits | |
| 1-7 days | 4 |
| >7 days | 1 |

*ECOG: Eastern Cooperative Oncology Group, MSCC: metastatic spinal cord compression, RT: radiotherapy

**≥24 points: 96.0% died within 2 months

been reported to have achieved a consistency rate of 90% or higher between the expected and actual survival periods on prospective analysis²). Therefore, which of the scoring systems is optimal remains uncertain.

There have been few reports on replication studies on the precision of prognostic scoring systems other than the Tokuhashi score and the subsequent Tomita score. Even the revised version of the Tokuhashi score was prepared more than 20 years previously and has become outdated in view of the prolonged survival state owing to advancements in treatments^{63,64}.

These scoring systems have been used for predicting life expectancy and selection of treatments⁶⁵, but they are also used to avoid overtreatment in patients with poor prognoses. Rades D et al. (2013)⁵⁶ evaluated risk factors of death within 2 months after radiotherapy and reported that mortality within 2 months was 96.0% with a specificity of 99.8% when the score was 24 or higher (Table 11).

There are also objections to limiting treatment options on the basis of a simple mathematical index provided by such a scoring system⁷⁰⁻⁷²). Gasbarrini A et al.^{70,71} stressed the importance of evaluation of individual patients in particular consideration of their sensitivity to adjuvant therapies and proposed a treatment algorithm emphasizing multidisciplinary

treatment selection incorporating a scoring system. Paton GR et al.⁷³ also proposed a therapeutic strategy in consideration of the tumor location level (L), mechanical instability (M), neurology (N), oncology (O), patient fitness, prognosis, and prior therapy (P).

Moreover, as functional prognosis depends on the survival period because of the nature of disease, these scoring systems are also used for predicting functional outcomes. Tang V et al. (2007)⁷⁴ used the Tokuhashi score to evaluate the indications for inpatient rehabilitation, because the score is correlated with the Functional Independence Measure (FIM) after rehabilitation. In addition, Yamashita T et al. (2008)⁷⁵ and Putz C et al. (2008)⁷⁶ reported that the Tokuhashi score can also be used for the prediction of functional recovery as it is correlated with neurological recovery. Rades D et al. also reported that walking ability after treatment could be predicted from survival factors of prognostic scores⁷⁷.

3) Future

As for the future of scoring systems, it is considered necessary to primarily adopt more oncological viewpoints, which are lacking in conventional scoring systems. Such viewpoints include 1) consideration of the stage and height of lesions, 2) evaluation of individual primary lesions, 3) addition of serum laboratory items as prognostic factors, and 4) consideration of multidisciplinary treatment, etc.

Concerning the stage of the disease, with advancements in the ability to detect metastases, features of metastatic spine tumors have been shown to change from the stage of progressive spinal cord paralysis and terminal stage to the asymptomatic stage, and it has become impossible to apply a single scoring system to all these stages. Scoring systems should be prepared and applied at least by clarifying the stage for which they are intended. Concerning the level of the lesion, it has been asserted that there is no appropriate scoring system for the cervical spine, which is an infrequent site of metastasis⁷⁸.

Regarding the evaluation of individual primary lesions, marked improvements in the prognosis of spinal metastasis have been observed owing to the rapid development of treatments in some cancers, and many authors have suggested that improvements in prognosis should be reflected in scoring systems^{25,79}). The necessity of scoring systems for specific cancer types has been maintained from before⁸⁰⁻⁸²), and scoring systems for specific types of cancer are expected to be increasingly prepared with accumulation of cases and systematization of treatments. For some cancer types, it is sufficiently possible to adopt specific tumor markers, etc., as prognostic factors. Crnalic S et al.⁵⁵ reported a scoring system for prostate cancer incorporating the prostate-specific antigen (Table 12)⁵⁵).

In addition, consideration of multidisciplinary treatments is required. Gregory TM et al. proposed that prognostic scoring systems should be changed by introducing anti-vascular endothelial growth factor (VEGF)⁸³). In the Lei score (2016)⁶⁴), which was reported recently, categorization of primary lesions by the Katagiri new score was adopted,

Table 12. Crnalic Score for Prostate Cancer Metastases (2012)⁵⁷⁾.

| Prognostic factor | Score (points) |
|---------------------|-------------------------|
| Hormone status | |
| Hormone native | 2 |
| Hormone refractory | 0 |
| KPS: (%) | |
| 80-100 | 2 |
| ≤70 | 0 |
| Visceral metastasis | |
| Absent | 1 |
| Present | 0 |
| PSA (ng/ml) | |
| Hormone native | 1 |
| Hormone refractory | |
| <200 | 1 |
| ≥200 | 0 |
| Total points | Median overall survival |
| 0-1 | 3 months |
| 2-4 | 16 months |
| 5-6 | 61.7 months |

*KPS, Karnofsky performance score; PSA, prostate-specific antigen

Table 13. Lei Score for Patients with MSCC after Surgical Decompression and Spine Stabilization and Outcomes (2016)⁶⁴⁾.

| Prognostic Factor | Scores (points) |
|-------------------------------------|-------------------|
| Primary site | |
| Slow growth | 2 |
| Moderate growth | 1 |
| Rapid growth | 0 |
| Preoperative ambulatory status | |
| Ambulatory | 2 |
| Not Ambulatory | 0 |
| Visceral metastases | |
| No | 3 |
| Yes | 0 |
| Preoperative chemotherapy | |
| No | 0 |
| Yes | 2 |
| Bone metastasis at cancer diagnosis | |
| No | 1 |
| Yes | 0 |
| Total points | 6 months survival |
| 0-2 (n=42) | 8.2% |
| 3-5 (n=90) | 56.5% |
| 6-10 (n=74) | 91.5% |

MSCC: Metastatic spinal cord compression

Slow growth: Hormone-dependent breast and prostate cancer, thyroid cancer, multiple myeloma, and malignant lymphoma

Moderate growth: Lung cancer treated with molecularly targeted drugs, hormone-independent breast and prostate cancer, renal cell carcinoma, endometrial and ovarian cancer, sarcoma, and others

Rapid growth: Lung cancer treated without molecularly targeted drugs, colorectal cancer, gastric cancer, pancreatic cancer, head and neck cancer, esophageal cancer, other urological cancers, melanoma, hepatocellular carcinoma, gallbladder cancer, cervical cancer, and cancers of unknown origin

the score allotment was changed for breast and prostate cancers depending on whether they are hormone-dependent or independent and for lung cancer depending on whether molecularly targeted drugs are used or not, and the history of chemotherapy was adopted as a prognostic factor.

Conclusion

These classification, evaluation, and scoring systems have been generally useful in the selection of suitable treatment strategies. However, we emphasize the necessity of multidisciplinary development and revision of classification and evaluation methods to adapt to the prolongation of survival associated with increased diversity and advancements of treatments.

Conflicts of Interest: The authors declare that there are no conflicts of interest.

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