Comparing prognostic factors in patients with spinal metastases: a literature review

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For cancer patients with spinal metastases, palliative treatments are directed toward improving the patient’s symptoms and quality of life. The expected prognosis of patients plays a large role in guiding treatment decisions, particularly when deciding between surgical management and conservative treatments, such as radiotherapy. This study aims to review the factors that can accurately predict the survival of patients with spinal metastases. The authors conducted a literature search on studies identifying prognostic factors using PubMed (1966–2011), Ovid MEDLINE (1948 to July 2011) and EMBASE (1947–2011) databases. Articles in English were included if they conducted retrospective or prospective analyses on predictors of survival for patients with spinal metastases; articles validating or examining the accuracy of existing scoring systems using prognostic factors were also included. A total of 29 studies were identified. A general consensus of the literature was found with respect to three prognostic factors: the patient’s primary cancer site, the extent of the metastases and the general condition or performance score. Further research is recommended to assess the prognostic value of other factors identified by several studies, including age, neurological deficit and previous treatments. For future studies, the authors encourage the development of models capable of inclusion of all patients with spinal metastases.

Keywords: prognostic factors • quality of life • spinal metastases

Approximately two-thirds of cancer patients will develop metastases in the bone [1,2]. A frequent site of bone metastases is the spine, which is diagnosed in 5–10% of advanced cancer patients and present in up to 90% of patients at autopsy [1,3]. Of patients with spinal metastases, 20% will develop spinal cord compression and its accompanying complications, including severe pain, neurological deficits, limited ambulatory function and paralysis [3,4]. Quality of life becomes a more meaningful and important end point when treatments are of palliative intent [1]. Available palliative treatment options for spinal metastasis include radiation therapy, systemic therapy and surgery [3]. The decision between various treatment modalities is a matter of optimizing the expected quality of life outcomes, while minimizing morbidity [4]. This decision is affected by a number of criteria, including the patient’s general level of health, the severity and nature of the metastases and the extent and anatomical behavior of the tumor [4]. The expected survival of the patient is also a significant factor that influences the decision-making process [4,5].

To date, many studies have addressed this issue by investigating prognostic factors and models that aid in estimating a patient’s survival and ultimately guiding palliative treatment decisions. There is little universal agreement across the literature on which factors are required to determine prognosis; this reveals a need for a clinically accurate and simple-to-use scoring system. The present review aims to accurately determine prognostic factors to predict the survival of patients with spinal metastases.

Methods
A literature review was conducted using PubMed (1966–2011), Ovid MEDLINE (1948 to July 2011) and EMBASE (1947–2011) databases to examine studies investigating factors that predict the survival of patients with spinal metastases. The search term ‘spinal metastases’ was combined with ‘prognosis’ or ‘survival’, as well as ‘factors’
or ‘predictors’ to elicit relevant literature. Reference lists of articles
found in the search were cross-referenced for additional pertinent
articles, and citations listed as ‘relevant’ in PubMed were also con-
sidered for review. Only peer-reviewed full texts were chosen for
possible inclusion.

The search revealed a total of 116 different articles from all
three databases and from cross-referring relevant citations.
Articles were included in the review if the study conducted
retrospective or prospective analyses on predictors of survival for
patients with spinal metastases. Articles validating or examining
the accuracy of existing scoring systems using prognostic factors
were also included. Potential sources of heterogeneity decided
a priori between studies were the type of study, approach, pur-
pose, statistical methods used, number of patients, primary cancer
site and median survival of patients, and prognostic factors were
extracted. Non-English studies were excluded.

Results
A total of 29 pertinent publications were identified and are
summarized in Table 1 [3–31]. Each study evaluated, in at least one
study arm, the prognostic factors of patients with spinal metas-
tases; however, there were four different approaches to this aim
among all 29 studies. The approach of seven studies was to design
either a prognostication model or a scoring system to predict survival
in patients with spinal metastases [7,8,10,13,15,20,21,22]. Another
12 studies externally validated previously developed prognosti-
cation models or scoring systems [5,16,19,22,23,25–31]. Five studies
identified prognostic factors of patients with spinal metastases
[3,4,9,14,18]. An additional five studies determined the survival of
a select cohort of spinal metastases patients [6,11,12,17,24].

Twenty-four of the 29 studies looked at heterogeneous samples
where patients have various primary tumor types [3–15,17,19–23,27–30],
whereas the remaining five examined only patients of one primary
site [16,18,24,26,31]. Two studies focused on lung cancer patients
[18,26], one study on a prostate cancer sample [24], one study examined a breast cancer sample [16] and another study looked specifically at hepatocellular carcinoma [31].

Prognostic factors for survival
The literature was relatively consistent with respect to three
prognostic factors. The type and location of the primary carci-
noma of the patient was identified as an important prognostic
parameter in 24 of the 25 studies that examined heterogeneous
samples [3–16,19–23,25–29]. Another 21 studies examined the severity of the patients’ metastases to be another predictive factor
[5,6,8,11,13–17,19,21–29], often concentrating on the extent of visceral
involvement [5,10,13,15,16,19,21–23,26,28–30]. Functional status was cited
as a predictive factor in 17 studies [4,5,13–16,18–23,25–29]; in 14 of
these studies, the Karnofsky Performance Status score was used
to measure functional status [4,5,13,15,16,19,20,22,23,25–29].

Apart from these three identified predictors, the literature
began to diverge in opinion with respect to other significant fac-
tors for prediction of survival. The age of the patient was identified
as a prognostic factor in five studies [11,12,17,20,21], and neurological
deficit was cited four times [4,6,12,17]. Factors surrounding previous
treatment appeared eight times in eight studies [3,4,11,14,20,21,23,25];
it included previous systemic treatment in three studies [4,21,23],
treatment of the primary tumor in three studies [3,20,25], previous
radiation treatment once [11] and persistence of the tumor after
radiation appeared once [14].

Validation of the accuracy of prognostic scoring systems
The scoring systems externally validated by the literature included
those developed by Sioutos et al. [7], Bauer and Wedin [8], van der
Linden et al. [13], Tokuhashi et al. [9] and Tomita et al. [10]. There
was no consensus about a preferred method in the literature.

The Tokuhashi scoring system, written in 1990 and revised
in 2005, appears frequently in the literature, with contradicting
opinions [4,5,15,16,18,19,22,23,26,28–31]. Four studies found the
Tokuhashi method to be reliable for the studied patient sam-
ples, of which three considered heterogeneous samples [9,22,29,31]
and one considered a breast cancer sample [16]. Three studies did
not find the Tokuhashi scoring method reliable, one of which
observed a heterogeneous sample [4] and two that examined a lung
cancer sample [18,26]. Furthermore, three studies found the
Tokuhashi method to be reliable, but preferred another method
[5,23,28]. Another study found the Tokuhashi method to be reliable
for breast and prostate cancer patients, somewhat reliable for colon
cancer patients and unreliable for lung and renal cancer patients
[30]. Of the remaining scoring systems, the van der Linden model
was validated in one study [27], and Bartels’ system was validated
in another [25]. Both of these studies examined heterogeneous
patient samples.

Results from studies in the literature using individual models
have been rather inconclusive regarding the superiority of one
scoring system over the other models available. Therefore, it is very
difficult to provide a generalized analysis indicating which model
is preferred. However, three studies were conducted comparing
all of the following scoring systems: Tokuhashi, Tomita, van der
Linden, Bauer and Sioutos [5,23,31]. Two of these studies reviewed
heterogeneous samples; they found the model by Bauer to be the
most reliable and the required information easy to collect [5,23].
The same two studies found the models by Tokuhashi, Tomita and
Sioutos to be less useful, and the model by van der Linden
to be less applicable as it did not easily accommodate patients
undergoing surgical intervention [5,23]. The third comprehensive
comparison was specific to a patient sample with hepatocellular
carcinoma [31]. This analysis found that the Tokuhashi and van
der Linden scoring methods were most accurate when revised to
include serum albumin and lactose dehydrogenase [31]. This study
found the model by Sioutos not to be applicable as the sample
studied for the Sioutos model did not represent patients with
hepatocellular carcinoma well [7,31]. The conclusions of these three
studies regarding the preference of one system over the others
have been based on the models’ ability to significantly distinguish
between distinct patient groups with varying prognosis.

Scientific analysis was conducted using statistical methods
in all original studies introducing new prognostication models
[7,8,10,13,15]. Bauer and Wedin used univariate analysis to determine
prognostic factors in patients with spinal metastases, and further

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<table>
<thead>
<tr>
<th>Study (year)</th>
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<th>Patients (n)</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Stark et al. (1982)</td>
<td>Retrospective</td>
<td>Determine the survival of a select cohort of patients</td>
<td>To analyze clinical elements of patients with spinal metastases to predict prognosis</td>
<td>$\chi^2$ test with Yates continuity correction where appropriate; Kendall’s $\tau$ and one-way analysis of variance for continuous data</td>
<td>131</td>
<td>Heterogeneous</td>
<td></td>
<td>Primary cancer site, nature of the underlying malignancy, extent of metastases and extent of neurological symptoms</td>
<td>[6]</td>
</tr>
<tr>
<td>Bauer and Wedin (1995)</td>
<td>Prospective</td>
<td>Design a prognostication model</td>
<td>To create a model to predict survival after surgical treatment of pathologic fractures for patients with spinal and extremity bone metastases</td>
<td>Kaplan–Meier analysis, Mantel–Haenzel test, Cox proportional hazards model and logrank test</td>
<td>241</td>
<td>Heterogeneous</td>
<td></td>
<td>Primary cancer site, extent of metastases and presence or absence of a pathologic fracture</td>
<td>[8]</td>
</tr>
<tr>
<td>Sioutos et al. (1995)</td>
<td>Retrospective</td>
<td>Design a prognostication model</td>
<td>To determine a method to predict survival in patients with epidural compression of the spinal cord from spinal metastases</td>
<td>Logrank test</td>
<td>109</td>
<td>Heterogeneous</td>
<td>10 months</td>
<td>Primary cancer site, extent of neurological symptoms and number of thoracic vertebrae with metastases</td>
<td>[7]</td>
</tr>
<tr>
<td>Nanassis et al. (1997)</td>
<td>Retrospective</td>
<td>Identify prognostic factors</td>
<td>To determine factors that can predict prognosis and indicate a need for surgical intervention of patients with spinal metastases</td>
<td></td>
<td>45</td>
<td>Heterogeneous</td>
<td></td>
<td>Primary cancer site, extent of metastases and time from symptom onset to diagnosis</td>
<td>[9]</td>
</tr>
<tr>
<td>Tomita et al. (2001)</td>
<td>Prospective/retrospective</td>
<td>Design a prognostication model</td>
<td>To develop a prognostic scoring system to determine surgical intervention strategies</td>
<td>Cox proportional hazards model</td>
<td>67</td>
<td>Heterogeneous</td>
<td></td>
<td>Primary cancer site, extent of visceral metastases and extent of bone metastases</td>
<td>[10]</td>
</tr>
</tbody>
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### Table 1. Summary of identified studies outlining prognostic factors in patients with spinal metastases (cont.).

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</thead>
<tbody>
<tr>
<td>Sundaresan et al. (2002)</td>
<td>Retrospective</td>
<td>Determine the survival of a select cohort of patients</td>
<td>Analysis of survival and neurological outcome after surgical intervention of patients with spinal epidural metastases to better plan future treatments</td>
<td>Kaplan–Meier analysis and χ² analysis</td>
<td>80</td>
<td>Heterogeneous</td>
<td>30 months</td>
<td>Age, primary cancer site, extent of metastases and previous irradiation</td>
<td>[11]</td>
</tr>
<tr>
<td>Finkelstein et al. (2003)</td>
<td>Retrospective</td>
<td>Determine the survival of a select cohort of patients</td>
<td>To evaluate potential predictors for survivorship and risk of complications for patients with spinal metastases undergoing surgery</td>
<td>Kaplan–Meier analysis. Cox proportional hazards model, multivariate logistic regression and multivariate linear regression</td>
<td>987</td>
<td>Heterogeneous</td>
<td>227 days</td>
<td>Age, gender, primary cancer site, and neurological deficit</td>
<td>[13]</td>
</tr>
<tr>
<td>Hirabayashi et al. (2003)</td>
<td>Retrospective</td>
<td>Identify prognostic factors</td>
<td>To relate treatment factors to survival and quality of life after surgical intervention for patients with spinal metastases</td>
<td>Kaplan–Meier analysis, Cox proportional hazards model, Mann–Whitney U test, Spearman's rank correlation coefficients and logrank test</td>
<td>81</td>
<td>Heterogeneous</td>
<td>10.6 months</td>
<td>Primary cancer site, postoperative ambulation and treatment of primary tumor</td>
<td>[3]</td>
</tr>
<tr>
<td>van der Linden et al. (2005)</td>
<td>RCT (multicenter)</td>
<td>Design a prognostication model</td>
<td>To develop guidelines for treating patients with spinal metastasis based on prognostic factors and response to radiotherapy</td>
<td>Kaplan–Meier analysis and Cox proportional hazards model</td>
<td>342</td>
<td>Heterogeneous</td>
<td>7 months</td>
<td>KPS, primary cancer site, and presence of visceral metastases</td>
<td>[13]</td>
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<tr>
<td>North et al. (2005)</td>
<td>Retrospective</td>
<td>Identify prognostic factors</td>
<td>To identify prognostic factors that can be used in a scoring system to predict neurological outcome and survival in patients with spinal metastases</td>
<td>Kaplan–Meier analysis and logrank test</td>
<td>61</td>
<td>Heterogeneous</td>
<td>10 months</td>
<td>Gender, primary cancer site, multilevel spinal surgery, recurrent/persistent disease after radiotherapy of operative site, location of spine metastases and preoperative ambulatory status</td>
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<tr>
<td>Tokuhashi et al. (2005)</td>
<td>Prospective/retrospective</td>
<td>Design a prognostication model</td>
<td>To evaluate the ability of a revised Tokuhashi scoring system to predict prognosis</td>
<td>Kaplan–Meier analysis</td>
<td>246</td>
<td>Heterogeneous</td>
<td>Mean: 8.7 months</td>
<td>KPS, primary cancer site, extent of extraspinal bone metastases, extent of vertebral metastases, extent of visceral metastases and extent of palsy</td>
</tr>
<tr>
<td>Ulmar et al. (2005)</td>
<td>Retrospective</td>
<td>External validation of a previously developed model</td>
<td>To compare the predicted survival using the Tokuhashi score with the true survival of breast cancer patients with spinal metastases</td>
<td>Kaplan–Meier analysis and logrank test</td>
<td>55</td>
<td>Breast</td>
<td>16.2 months</td>
<td>KPS, primary cancer site, extent of extraspinal bone metastases, extent of vertebral metastases, extent of visceral metastases and extent of palsy</td>
</tr>
<tr>
<td>Chow et al. (2006)</td>
<td>Prospective</td>
<td>External validation of two previously developed models</td>
<td>To externally validate the Dutch Bone Metastases Study Group model of predicting the survival of patients with spinal bone metastases, and compare it with the RRRP’s model</td>
<td>Risk group stratification</td>
<td>231</td>
<td>Heterogeneous</td>
<td>7 months</td>
<td>RRRP: KPS, primary cancer site and location of metastases; ESAS scores: fatigue, appetite and shortness of breath; and Dutch Bone Metastases Study Group model: KPS, primary cancer site and visceral involvement</td>
</tr>
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## Table 1. Summary of identified studies outlining prognostic factors in patients with spinal metastases (cont.).

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<tbody>
<tr>
<td>Jansson and Bauer (2006)</td>
<td>Prospective</td>
<td>Determine the survival of a select cohort of patients</td>
<td>To examine surgical intervention to restore neurological function to patients with spinal metastases</td>
<td>Kaplan–Meier analysis</td>
<td>282</td>
<td>Heterogeneous</td>
<td></td>
<td>Age, neurological deficit, and extent of bone metastases</td>
<td>[17]</td>
</tr>
<tr>
<td>Oghihara et al. (2006)</td>
<td>Retrospective</td>
<td>Identify prognostic factors</td>
<td>To use clinical data to create criteria to aid in the decision of surgical intervention for lung cancer patients with spinal metastases and compare to the Tokuhashi scoring system</td>
<td>Kaplan–Meier analysis, logrank test and Cox proportional hazards model</td>
<td>114</td>
<td>Lung</td>
<td>4.52 months NSCLC: 4.93 months SCLC: 5 months</td>
<td>Postoperative ECOG PS serum calcium level, serum albumin level and previous systemic therapy</td>
<td>[18]</td>
</tr>
<tr>
<td>Bartels et al. (2007)</td>
<td>Retrospective</td>
<td>Design a prognostication model</td>
<td>To develop a prediction model to accurately estimate the survival of patients with spinal metastases</td>
<td>Cox proportional hazards model, logrank test, $R^2$ Nagelkerke, concordance index and Efron optimism correction</td>
<td>219</td>
<td>Heterogeneous</td>
<td>3 months</td>
<td>Gender, KPS, primary cancer site, intended treatment of primary tumor and cervical location of spinal metastases</td>
<td>[20]</td>
</tr>
<tr>
<td>Ulmar et al. (2007)</td>
<td>Retrospective</td>
<td>External validation of a previously developed model</td>
<td>To evaluate the Tokuhashi scoring method (original and revised) in predicting survival in patients with spinal metastases</td>
<td>Kaplan–Meier analysis and logrank test</td>
<td>217</td>
<td>Heterogeneous</td>
<td>8 months</td>
<td>KPS, primary cancer site, extent of extraspinal bone metastases, extent of vertebral metastases, extent of visceral metastases and extent of palsy</td>
<td>[19]</td>
</tr>
<tr>
<td>Leithner et al. (2008)</td>
<td>Prospective/retrospective</td>
<td>External validation of seven previously developed models</td>
<td>To evaluate seven methods of predicting survival after surgery of patients with spinal metastases</td>
<td>Kaplan–Meier analysis, logrank test and Cox proportional hazards model</td>
<td>69</td>
<td>Heterogeneous</td>
<td>14 months</td>
<td>KPS (for myeloma patients only), primary cancer site and presence of visceral metastases</td>
<td>[5]</td>
</tr>
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<tbody>
<tr>
<td>Mizumoto et al. (2008)</td>
<td>Retrospective</td>
<td>Design a prognostication model</td>
<td>To develop a scoring system using prognostic factors to predict survival of patients with spine metastases</td>
<td>Cox proportional hazards model, K-means clustering method and logrank test</td>
<td>544</td>
<td>Heterogeneous</td>
<td>5.9 months</td>
<td>Age, ECOG PS, primary tumor type, extent of bone metastases, presence of visceral metastases, previous systemic therapy and total serum calcium corrected for albumin level</td>
<td>[21]</td>
</tr>
<tr>
<td>Tokuhashi et al. (2009)</td>
<td>Prospective</td>
<td>External validation of a previously developed model</td>
<td>To evaluate the ability of the Tokuhashi scoring system to be used as a treatment strategy for patients with spinal metastases</td>
<td>Fisher’s exact test and Pearson χ² test</td>
<td>183</td>
<td>Heterogeneous</td>
<td></td>
<td>KPS, primary cancer site, extent of extraspinal bone metastases, extent of vertebral metastases, presence of visceral metastases and extent of palsy</td>
<td>[22]</td>
</tr>
<tr>
<td>Wibmer et al. (2011)</td>
<td>Retrospective</td>
<td>External validation of seven previously developed models</td>
<td>To compare seven prognostic scoring systems by their ability to predict survival in patients with spinal metastases</td>
<td>Kaplan–Meier analysis and Cox proportional hazards model</td>
<td>254</td>
<td>Heterogeneous</td>
<td>10.6 months</td>
<td>KPS, primary cancer site, presence of visceral metastases and previous systemic therapy</td>
<td>[23]</td>
</tr>
<tr>
<td>Chen et al. (2010)</td>
<td>Retrospective</td>
<td>External validation of five previously developed models</td>
<td>To compare the accuracy of five scoring systems and determine prognostic factors to predict survival of hepatocellular carcinoma patients with spinal metastases</td>
<td>Kaplan–Meier analysis, logrank test and Cox proportional hazards model</td>
<td>41</td>
<td>Hepatocellular carcinoma</td>
<td>10.4 months</td>
<td>KPS, extent of spinal metastases, serum albumin and serum lactose dehydrogenase</td>
<td>[31]</td>
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<tr>
<td>Drzymalski et al. (2010)</td>
<td>Retrospective</td>
<td>To determine the survival of a select cohort of patients</td>
<td>Determine factors to predict survival of prostate cancer patients at the time of diagnosis of spinal metastases</td>
<td>Kaplan–Meier analysis, Cox proportional hazards model and logrank test</td>
<td>333</td>
<td>Prostate</td>
<td>24 months</td>
<td>PSA level at diagnosis, extent of metastases, and time between prostate cancer diagnosis and spinal metastases diagnosis</td>
<td>[24]</td>
</tr>
<tr>
<td>Bartels et al. (2011)</td>
<td>RCT (multicentre)</td>
<td>External validation of a previously developed model</td>
<td>To externally validate a model to predict the survival of patients presenting with spinal epidural metastases</td>
<td>Concordance index and R² Nagelkerke</td>
<td>356</td>
<td>Heterogeneous</td>
<td>6.1 months</td>
<td>Gender, KPS, primary cancer site, intended treatment of primary tumor and extent of metastases</td>
<td>[25]</td>
</tr>
<tr>
<td>Hessler et al. (2011)</td>
<td>Retrospective</td>
<td>External validation of a previously developed model</td>
<td>To evaluate the Tokuhashi scoring method for predicting the survival of lung cancer patients with spinal metastases</td>
<td>Fisher’s exact test</td>
<td>76</td>
<td>Lung</td>
<td>3.6 months</td>
<td>KPS, extent of extraspinal bone metastases, extent of vertebral metastases, presence of visceral metastases and extent of palsy</td>
<td>[26]</td>
</tr>
<tr>
<td>Padalkar and Tow (2011)</td>
<td>Retrospective</td>
<td>External validation of two previously developed models</td>
<td>To determine criteria to predict survival in patients with spinal metastases, including Tokuhashi score, Tomita score and other variables</td>
<td>Kaplan–Meier analysis, logrank test and Cox proportional hazards model</td>
<td>102</td>
<td>Heterogeneous</td>
<td>7 months</td>
<td>KPS, extent of visceral metastases, extent of bone metastases, Tokuhashi score and Tomita score</td>
<td>[28]</td>
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<tr>
<td>Pointillart et al. (2011)</td>
<td>Prospective</td>
<td>Identify prognostic factors</td>
<td>To investigate prognostic factors and Tokuhashi scores with respect to clinical outcomes in patients with spinal metastases</td>
<td>Kaplan–Meier analysis, logrank test and Cox proportional hazards model</td>
<td>142</td>
<td>Heterogeneous</td>
<td>5 months</td>
<td>KPS, ASA score, Tokuhashi score, primary cancer site, pain levels, vascular or pulmonary disease, previous systemic therapy, neurological deficit and weight lost 6 months prior to surgery</td>
<td>[4]</td>
</tr>
<tr>
<td>Wang et al. (2011)</td>
<td>Prospective</td>
<td>External validation of a previously developed model</td>
<td>To evaluate the accuracy of the Tokuhashi scoring system</td>
<td>Kaplan–Meier analysis, logrank test and McNemar’s test</td>
<td>448</td>
<td>Heterogeneous</td>
<td>6.8 months</td>
<td>KPS, primary cancer site, extent of extraspinal bone metastases, extent of vertebral metastases, presence of visceral metastases and extent of palsy</td>
<td>[30]</td>
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<td>Yamashita et al. (2011)</td>
<td>Prospective</td>
<td>External validation of a previously developed model</td>
<td>To define the use of the revised Tokuhashi score to predict the survival of patients with spinal metastases</td>
<td>Kaplan–Meier analysis, Pearson correlation coefficient, Cox proportional hazards model, Spearman’s rank correlation coefficient, logrank test and student’s t-test</td>
<td>85</td>
<td>Heterogeneous</td>
<td>11.6 months</td>
<td>KPS, primary cancer site and presence of visceral metastases</td>
<td>[29]</td>
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</table>

used the Cox proportional hazards model to discern whether these factors had a positive or negative prognostic influence on the 1-year survival of patients [8]. Sioutos et al. determined their prognostic factors by means of a logrank test for unpaired data. A p-value ≤ 0.05 was considered statistically significant [7]. The study by Tomita et al. considered three potential prognostic factors in its evaluation: the grade of malignancy of the primary tumors; the visceral metastases to vital organs (lungs, liver, kidneys and brain); and bone metastases [10]. They then used the Cox proportional hazards model to assign value to each of the identified prognostic factors. Similar to the method used by Tomita et al. [10], Van der Linden et al. studied a collection of patient characteristics for their use in prediction of patient survival: primary tumor; Karnofsky Performance Status score; extent of visceral involvement; solitary versus multiple bone metastases; and response to radiotherapy [13]. They then used the Cox proportional hazards model to analyze univariate and multivariate data. Tokuhashi et al. [5] aimed to revise a former prognostication model, and as such did not make use of any statistical or scientific analysis when determining the value of prognostic factors, but rather relied on the statistical evidence from their original study in 1990 [32].

Discussion
Radiation therapy, systemic therapy and surgery are among the several palliative treatments available for patients with spinal metastases. Many criteria must be considered when making treatment decisions and when choosing how conservative certain treatment methods should be. Factors that are commonly included in the decision-making process are the patient’s general level of health, the severity and nature of the metastases and the extent and anatomical behavior of the tumor [4]. The expected survival of the patient is another significant determinant that must be taken into consideration during this decision-making process [4,5]. Studies in the literature investigated and proposed predictive factors of survival in this patient population; there is great consensus on certain factors that are required to make these predictions, but a divergence on others. This suggests a need for a universally accepted scoring system that incorporates the predicted prognosis of these patients [5,8,24–26]. Currently in the literature, no method has proven to be robust enough to accommodate the entire spinal metastasis patient population [30].

It is clear from the lack of consensus in the literature that a current model satisfactory to analyze all patients with spinal metastases does not exist [4,18,26,30,31]. The agreement of the literature has indicated three parameters that are vital to an accurate model: the site of the primary tumor, the extent of the patients’ metastases and the performance status of the patient. These factors will most likely remain important in the development of a model that is accurate among all patients with spinal metastases.

The revised Tokuhashi scoring system has been proven to perform well for patients whose primary cancer site is breast or prostate [16,30]. It is less effective for patients with lung or kidney as a primary cancer site [18,26,30]. The Tokuhashi model has inconsistent accuracy when analyzing heterogeneous populations; this can possibly be attributed to the variation in the composition of the populations [4,19,22,28–30]. The Bauer model showed the highest accuracy of all of the examined models when assessing a heterogeneous patient population [5,23]. The authors recommend all prognostic models to be validated in independent datasets.

The development of a model that is accurate for all patients requires future work. The factors that are partially agreed on by the literature with respect to predictive contribution should be investigated further to develop a consensus on their use in future models. These three identified predictors are age, neurological deficit and previous treatment methods. These factors and any other applicable factors should be used to customize existing models for specific patient populations, such as the hepatocellular carcinoma patients in the study by Wang et al., or to create a new model [30]. Once a model is developed, it must be validated against the patient population for which it is intended.

One of the limitations of this review is that only English language articles were used. There was a lack of primary site-specific resources to contribute to this analysis, and it was dominated by heterogeneous populations. The study did not distinguish between patients with signs of spinal cord compression or cauda equina syndrome and patients without radiculopathy or myelopathy. This is a possible reason why neurological deficit was found not to be a consistent prognostic factor in the literature. Furthermore, the heterogeneity in aims of the various studies limits the review.

Conclusion
A model for assessing the prognosis of patients with spinal metastases is essential for determining how to manage palliative care [5,8,24–26]. The literature agrees on several factors that have been proven to contribute to the patient’s treatment plan: primary cancer site, extent of metastases and performance score. Factors to be investigated further include age, neurological deficit and previous treatments. Future studies should also examine the role of new prognostic factors that have not been considered in patient populations to date. For example, mechanical compression due to collapsed vertebrae and the use of corticosteroids are two factors that should be analyzed for their prognostic value.

No current scoring system is robust enough to accommodate all patients with spinal metastases [30]. The Tokuhashi model shows promise for predicting prognosis of patients with breast or prostate as the primary cancer site, but is less effective for patients with the lung or kidney as the primary cancer site. In comparison with all of the current models, the Bauer model performs well. The authors encourage investigators to further analyze which prognostic factors are optimal for predicting survival among all patients with spinal metastases. The ideal approach would be to apply individual models on independent datasets directly. In addition, further analyses should examine the usefulness of each prognostic factor in terms of the properties that govern each factor, including discrimination, calibration, generalizability, simplicity and reproducibility. Future studies...
aimed toward developing new scoring systems that are of use in predicting survival for the entire spinal metastasis patient population, based on currently available methods, would also prove valuable. As models thus far provide an overall score based on the included variables, the individual prognostic significance of each item is not known. Future studies are recommended to investigate the relative predictive strength of individual factors of these prognostic models.

Expert commentary
The expected prognosis of patients with spinal metastases plays a large role in guiding treatment decisions, particularly when deciding between surgical management and conservative treatments such as radiotherapy. Thus far, there have been a total of 29 studies in the literature that investigate factors used to predict survival of patients with spinal metastases. A compilation of these factors is needed to identify which ones must be used by medical professionals when selecting treatment decisions.

Key issues
- The expected prognosis of patients with spinal metastases plays a large role in guiding treatment decisions.
- Factors that predict survival in patients with spinal metastases were identified in 29 studies.
- A compilation of these factors is needed to identify which ones medical professionals should use when making treatment decisions.
- A general consensus of the literature was found with respect to three prognostic factors: the patient’s primary cancer site, the extent of the metastases, and the general condition or performance score.
- No current scoring system is robust enough to accommodate all patients with spinal metastases.
- Future studies should further investigate other factors, such as age, neurological deficit and previous treatments to specific patient populations. It is hoped that this information will be vital to developing a universal scoring system that will aid healthcare professionals in making a more informed selection of the most appropriate treatment modality for the individual patient.

References
Papers of special note have been highlighted as:
• of interest
** of considerable interest


Five-year view
The literature agrees on several factors that have been proven to contribute to the patient’s treatment plan, including primary cancer site, extent of metastases and performance score. Future studies should further investigate other factors, such as age, neurological deficit and previous treatments to specific patient populations. These recommendations will be vital to establishing a universal scoring system that will aid healthcare professionals in making a more informed selection of the most appropriate treatment modality for the individual patient.

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