Tokuhashi score and other prognostic factors in 260 patients with surgery for vertebral metastases

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ABSTRACT

Background: Metastatic disease of the spine is an increasingly common public health problem. Surgery should be an integral component of the overall cancer treatment plan and, importantly, must neither delay nor jeopardize any of the other components. The prognosis governs the choice of the surgical strategy. Tokuhashi et al. developed a prognostic score in 1990, then revised it in 2000 and 2005. Here, our objective was to evaluate the performance of the Tokuhashi score in a cohort of 260 patients and to look for other variables that might improve preoperative outcome prediction.

Material and method: We retrospectively established a single-centre cohort of 260 patients who underwent spinal metastasis surgery between 1998 and 2008. For each patient, the following data were collected prospectively: socio-demographic features, history of the malignancy, variables needed to determine the Tokuhashi score, and treatments used. SAS 9.0 software was chosen for the statistical analysis. Variables were described as mean ± SD, overall survival was estimated using the Kaplan–Meier method, and survivals in subgroups were compared by the log-rank test. To assess agreement between survival predicted by the Tokuhashi score and observed survival, we computed Cohen’s kappa and interpreted the results according to Landis and Koch.

Results: There were 143 females and 117 males with a mean age of 59 years and overall median survival of 10 months. Median observed survivals in the three Tokuhashi score categories (<6, 6–12, and > 12 months predicted survival) were 5, 10, and 36 months, respectively. These survival times differed significantly (P < 0.0001). Cohen’s kappa indicated moderate agreement between predicted and observed survivals. Other factors associated with significant survival differences were time from cancer diagnosis to metastasis diagnosis (synchronous, < 2 years, 2–5 years, or > 5 years; P = 0.0001) and age (< 70 years or ≥ 70 years, P = 0.0053).

Conclusion: Our cohort study supports the validity and reproducibility of the Tokuhashi score. Our finding that shorter time to metastasis diagnosis and age ≥ 70 years were also significantly associated with survival in our population invites further efforts to improve and update the Tokuhashi score.

Level of evidence: IV, retrospective study.

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1. Introduction

Spinal tumours, particularly metastases, constitute an increasingly common public health problem. Among causes of paraplegia, tumours now tend to be at least as common than injuries [1,2]. In addition, the development of a major neurological impairment often leads to the discontinuation of cancer treatments.

The objectives of spinal metastasis therapy are functional and include improving quality of life; preventing or improving neurological function, which requires a careful evaluation of the neurological risk before impairments develop; ensuring stability of the spine; alleviating the pain; and avoiding the need for external immobilisation devices. The overall goal is to allow the patient to remain self-sufficient and capable of living at home for as long as possible.

Achieving these objectives requires a multidisciplinary approach in which the surgeon plays a major role. If surgical management is deemed appropriate, it must neither delay nor jeopardise the other components of the cancer treatment plan.
The prognosis in each individual patient is a key factor in choosing the best surgical strategy. In 1990, Tokuhashi et al. developed a score for predicting the outcomes of spinal metastases [3]. They revised their score in 2000 [4] and 2005 [5]. The score uses six variables to classify patients into three prognostic categories with predicted survival times of less than 6 months, 6 to 12 months, and more than 12 months, respectively. The category provides some measure of guidance for selecting the surgical strategy [5].

Here, our objectives were to evaluate the predictive performance of the Tokuhashi score in a cohort of 260 patients and, importantly, to look for other factors that further improved outcome prediction, thereby providing additional guidance about the best surgical treatment.

2. Material and methods

2.1. Patients

We retrospectively established a cohort of 260 patients who underwent spinal metastasis surgery at the neurosurgery department of the Foch Hospital, Suresnes, France, between 1998 and 2008. Inclusion criteria were age older than 18 years, metastatic spinal disease requiring surgical treatment (e.g., nerve root or spinal cord compression, risk of neurological compromise), and willingness to participate in the study. We did not include patients younger than 18 years of age, under guardianship, or having missing data. Exclusion criteria were non-metastatic spinal tumors (e.g., primary tumors or spinal involvement with haematological malignancies), history of spinal biopsy, and in-dural metastases.

2.2. Data collection

We recorded the following data for each patient: age and gender, circumstances of spinal metastasis diagnosis, time from diagnosis of the primary to diagnosis of the spinal metastases, variables needed to compute the 2005 version of the Tokuhashi score [5], and characteristics of the treatment (e.g., surgical approach, operative technique, and preoperative or postoperative radiotherapy). The data were recorded at the time of death in non-survivors and 60 and 110 months after spinal metastasis surgery in survivors.

2.3. Statistical analysis

We used SAS 9.0. software (SAS Institute, Cary, NC, USA) for the statistical analyses. Qualitative variables were described as mean ± SD and qualitative variables as n (%).

Kaplan–Meier curves were plotted to estimate overall survival, with the date of spinal metastasis surgery as the starting point and death as the end point. Survival across groups was compared using the log-rank test.

We evaluated the level of agreement between survival predicted by the Tokuhashi score and observed survival. To this end, we computed Cohen’s kappa coefficient (κ) [6] and interpreted the results according to Landis and Koch [7].

3. Results

3.1. Patient population

We identified 260 patients, 143 (55%) females and 117 (45%) males with a mean age of 59 ± 11 years (range, 24–81 years). Table 1 reports the sites of the primary malignancies. For each patient, the appropriateness of spinal metastasis surgery was evaluated in a multidisciplinary meeting. Criteria for palliative surgery were spinal cord compression; nerve root compression; pain; risk of neurological compromise, most notably related to spinal instability; and an expectation that spinal surgery would improve the oncological prognosis. Excisional surgery was considered appropriate only when a slowly growing solitary spinal metastasis was present in a young patient. Of our 260 patients, 17 underwent excisional surgery and 243 palliative surgery.

The surgical approach and operative technique were chosen based on the vertebral segment involved, number of vertebral metastases, and general health condition of the patient. Intraoperative vertebroplasty was performed in 82 (31.5%) patients. Other procedures were posterior decompression with internal fixation (56%), anterior decompression with internal fixation (37%), decompression alone (5%) and vertebrectomy (2%).

3.2. Survival predicted by the Tokuhashi score and observed survival

Overall mean survival was 10 months. Of the 260 patients, 212 (82%) died within 60 months of spinal metastasis surgery.

Table 2 reports the values for each of the Tokuhashi score items. Patient distribution in the three prognostic groups defined by the Tokuhashi score was as follows: score 0–8 (predicted survival < 6 months), 105 (40.4%) patients; score 9–11 (predicted survival > 6 months), 82 (31.5%) patients; and score 12–15 (predicted survival > 12 months), 73 (28.1%) patients.

Table 3 reports predicted and observed survivals. Observed median survival in the 0–8, 9–11, and 12–15 Tokuhashi score groups was 5 months (95% CI, 3–6), 10 months (95% CI, 8–19), and 36 months (95% CI, 30–54), respectively. Fig. 1 displays the survival curves. Survival differed significantly across the three groups (P < 0.0001).

The weighted κ computed to assess agreement between survival predicted by the Tokuhashi score and observed survival was 0.41 (95% CI, 0.33–0.50). According to Landis and Koch [7], this κ value indicates moderate agreement.

We classified tumour histology according to the system used for the Tokuhashi score. Table 1 reports the results. Kaplan–Meier survival estimates differed significantly across histological groups (P < 0.0001).

Median survival differed significantly according to the Frankel grade function (P = 0.0001), as follows: Frankel E, 16 months (95% CI, 11–25); Frankel C-D, 6 months (95% CI, 4–9); and Frankel A-B, 4 months (95% CI, 1–7). The very short survival in the Frankel A-B group, which we believe contra-indicates surgery, emphasises the importance of preventing neurological impairments and evaluating the risk of neurological compromise.

### Table 1

<table>
<thead>
<tr>
<th>Primary tumours</th>
<th>Lung</th>
<th>Prostate</th>
<th>Breast</th>
<th>Colorectal</th>
<th>Kidney</th>
<th>Bladder</th>
<th>Other</th>
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3.3. Identification of additional predictors of survival

We separately evaluated the potential association with survival of the parameters listed in Table 4. As illustrated by Fig. 2, age ≥ 70 years was associated with significantly shorter survival (P = 0.0053). Although not among the Tokuhashi score items, age is, in our opinion, a major consideration when making surgical decisions in everyday practice and should be factored into the preoperative evaluation.

The time in months from diagnosis of the primary to diagnosis of spinal metastatic disease was available for all patients. We converted this continuous variable into four categories, as
follows: 0 \((n = 79, 30.4%)\), \(\leq 2\) years \((n = 56, 21.5\%)\), 2–5 years \((n = 66, 25.4\%)\), and \(> 5\) years \((n = 59, 22.7\%)\). Survival as assessed using Kaplan–Meier curves differed significantly across these four groups (log-rank test, \(P < 0.0001\)) (Fig. 3).

Table 4 lists the spinal segments involved. Comparison of survival curves across the seven groups failed to detect any significant difference (log-rank test, \(P = 0.29\)). Thus, the spinal segment involved with metastatic disease does not affect survival. Nevertheless, the site of the metastasis influences the risk of neurological compromise and the feasibility of surgical treatment. For instance, with metastases in the cervical spine, the major risk of severe neurological compromise and ease of access, particularly via the anterior approach, encourage an aggressive surgical strategy. Challenges raised by ensuring spinal stability are greatest at the junctions, most notably between the cervical and thoracic spine.

4. Discussion

The surgical management of spinal metastases has been the focus of much controversy. In a 1979 prospective randomised trial (level 1 evidence) by Young and Feldman, 16 patients managed with radiotherapy and laminectomy had no significant outcome differences compared to 13 patients managed with radiotherapy alone [8]. Despite the small numbers of patients in both groups and the short follow-up of only 4 months, this trial generated a strong belief that surgery was unhelpful in spinal metastases. Since then, many small case-series studies have suggested beneficial effects of surgery. However, not until 2005 was a new prospective randomised trial reported, by Patchell et al., who studied 123 patients distributed into two comparable groups [9]. The trial was stopped prematurely when an interim analysis showed significantly better outcomes with combined surgery and radiotherapy compared to radiotherapy alone.

Accurate outcome prediction is crucial for determining the best surgical strategy in patients with spinal metastases. Also of importance are the benefits expected by the patient and the risk of complications, as postoperative complications can cause rapid deterioration in these fragile patients [10–12]. Survival in patients with spinal metastases has therefore been the focus of numerous studies, which produced variable results. In a 1996 report by Tatsui et al. of patients with spinal metastatic disease diagnosed by bone scintigraphy, 1-year survival varied across primary tumour sites, as follows: 83.3% for prostate cancer, 77.7% for breast cancer, 51.2% for kidney cancer, 21.7% for lung cancer, and 0% for stomach cancer [13].

Major strengths of our study include the large sample size \((n = 260)\) and 10-year follow-up. We found no previously published studies of larger populations with surgically treated spinal metastases. No selection bias occurred, as we included all patients who underwent spinal metastasis surgery in our department during the study period. Although the data were analysed retrospectively, they were collected prospectively.

Our results support the validity of the Tokuhashi score for predicting outcomes in patients with spinal metastases. The level of agreement between outcomes predicted based on the Tokuhashi score and observed outcomes were moderate, as assessed according to Landis and Koch. We believe this level of agreement is largely satisfactory in clinical practice.

We obtained two unexpected results. First, median survival was longer in patients with inoperable internal organ metastases than in patients with no internal organ metastases (Table 1). Two factors may explain this finding, namely, the small number of patients with internal organ metastases \((n = 23)\) and the predominance among them of primaries associated with long survival times (breast cancer, \(n = 14\); prostate cancer, \(n = 4\); lung cancer, \(n = 2\); stomach cancer, \(n = 1\); urinary bladder cancer, \(n = 1\); and other, \(n = 1\)). Second, survival was short among patients with metastases from rectal cancer. This result may be ascribable to the small number of patients in this subgroup \((n = 11)\).

The Tokuhashi score was first reported in 1990 [3], then used, analysed, and validated in several studies [12,14–16]. Neurological
impairments had no adverse prognostic significance in some studies [17,18]. Nevertheless, our patients with neurological impairments had significantly worse outcomes, in keeping with a study of 200 patients reported by Arrigo et al. [19]. In 1997, Enkaoua et al. suggested changing the number of points for metastases from unidentified primaries from 1 to 0 [20]. Our findings support this suggestion.

In 2001, Tomita et al. reported another scoring system based on three prognostic factors: grade of the malignancy, number and treatability of visceral metastases, and number of bone metastases [17]. Their rationale for developing a new score was that the Tokuhashi score distinguishes only two treatment options, excisional and palliative surgery, instead of considering the full range of currently available surgical strategies.

Two 2007 reports by Ulmar et al. assess the Tokuhashi [16] and Tomita [21] scores in a cohort of 217 patients with vertebral metastases. Their results validate the Tokuhashi score and establish its superiority over the Tomita score for predicting survival. Similarly, in 2013, Quraishi et al. reported that the Tokuhashi score provided valuable guidance for surgical decision-making [12].

We believe the Tokuhashi score alone is not sufficient to select patients for excisional surgery. The appropriateness of excisional surgery should be discussed in a multidisciplinary meeting based on a range of characteristics including age and tumour aggressiveness. Of our 260 patients, 17 underwent excisional surgery. Their median survival was 84 months (95% CI, 41–96). Palliative surgery was performed in 243 patients, whose median survival was 9 months (95% CI, 8–11). The survival curves differed significantly between these two groups (P < 0.0001).

Patient age at surgery emerged as a major prognostic factor. As a corollary to the ageing of the general population, age at management tends to increase. Thus, surgeons are increasingly assessing elderly patients referred for the management of spinal metastases. In a study by Arrigo et al. [19], age was a significant predictive factor when incorporated into the Charlson Comorbidity Index [22], but not when considered alone. In our study, age ≥ 70 years was significantly associated with shorter survival.

Another important prognostic factor in our study was the time from the diagnosis of the primary to the diagnosis of spinal metastatic disease. According to the log-rank test, survival times differed significantly (P < 0.0001) across the four primary to metastasis interval groups distinguished in our study (synchronous, < 2 years, 2–5 years, and > 5 years). The Kaplan–Meier analysis also indicated markedly shorter survival times among patients with early metastases. These findings confirm the poor prognostic significance of early metastases. In contrast, patients with delayed metastatic disease deserve to be considered for more radical excisional procedures.

Patients with synchronous metastases had longer survival times compared to those with metastases diagnosed within 2 years of the primary in our study. This finding is clearly ascribable to the good prognosis of the primaries responsible for synchronous metastases, which responded well to systemic therapy. In contrast, patients diagnosed with metastases disease within the first 2 years developed these tumours despite systemic treatment for the primary. Our data support the importance in everyday practice of the time to metastasis diagnosis when selecting the surgical strategy.

Our findings confirm the validity of the Tokuhashi score as a prognostic tool for patients with spinal metastases, in agreement with earlier studies. Nevertheless, we believe the Tokuhashi score should be updated by adding variables, such as age ≥ 70 years and time to metastasis diagnosis, which were significantly associated with survival in our study. The steady pace of progress in the therapeutic weaponry available for cancer treatment requires regular reappraisals of prognostic tools. Non-operative treatments are increasingly used in a targeted manner, most notably according to the histological tumour type. The histological classification used in the Tokuhashi score may now appear simplistic. Among surgical procedures, percutaneous internal fixation techniques developed to treat spinal injuries have a broad range of applications in spinal metastasis surgery. For instance, minimally invasive stabilisation procedures can be used for patients who are not candidates for open palliative surgery. Although few published data are available on this point, we believe that percutaneous techniques have a role to play in spinal metastasis surgery [23]. Finally, stereotactic radiotherapy of the spine is developing at a brisk pace. This method allows the delivery of higher doses to the tumour while sparing the adjacent structures, such as the nervous system [24–26], a property that would be expected to optimise post-radiotherapy outcomes.

This array of recent advances offers hope for improving patient outcomes and supports the need for studies aimed at optimising current prognostic scores.

5. Conclusion

Our cohort study confirms the validity and reproducibility of the Tokuhashi score for outcome prediction in patients with spinal metastatic disease. Nevertheless, two additional variables, age ≥ 70 years and time to metastasis diagnosis, were significantly associated with survival in our population. These variables deserve to be incorporated into tools designed to predict outcomes in patients with spinal metastases.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References


