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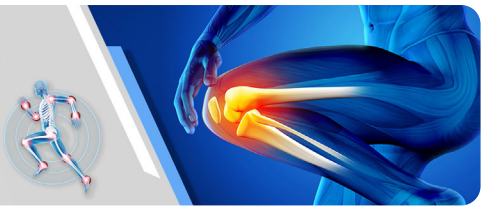

Reliability of the Modified Tokuhashi Score for Decision-Making in Patients Surgically Treated for Thoracolumbar Spine Metastasis – Experience in a Single-Center

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Abstract

Background: Oncological patients frequently suffer from spinal metastases. The decision to perform surgery mostly rely over scoring systems that could be outdated.

Methods: A retrospective study of 60 patients was performed, wherein different scoring methods were used and compared to evaluate their accuracy in predicting survival for patients who underwent spinal surgery. Patient scoring systems were assessed by ROC curve, Kaplan-Meier, and Cox proportional hazard regression analyses.

Results: The performance of the modified Tokuhashi score was only marginally better than that of a random classifier, but Kaplan-Meier curves of the Tomita and modified Tokuhashi scores exhibited statistically significant differences between different score groups according to the log-rank test. The univariate analysis revealed the statistical significance of a small set of factors for predicting patient survival, and the multivariate analysis revealed the statistical significance of an even smaller set of factors. Neither prior nor ongoing immuno/hormonotherapy significantly improved patient survival, but patients with prostate or breast primary tumors nonetheless appeared to have a slightly better likelihood of long-term survival.

Conclusion: In total, patient scoring systems have only demonstrated mediocre reliability for predicting survival following spinal surgery. The overall heterogeneity of patient profiles requires nuanced and tailored decision-making, and current scoring systems can at most provide very weak guidance in this process.

Keywords: Spinal metastases; Modified Tokuhashi score; Surgical decision-making; Prognostic scores

Introduction

The management of metastatic spinal disease has changed drastically over the last few years. The use of recent technological advances in spinal surgery, along with an explosive assortment of medical treatment options, such as chemotherapy, radiotherapy, hormonotherapy, and immunotherapy, are changing the prognosis for these patients. Spinal metastasis is common among cancer patients [1]. Surgery may not always be the best treatment option when taking the likelihood of survival and quality of life into account. However, several clear indicators for surgery exist, such as pain, growing tumors that are resistant to therapy, spinal cord tolerance, spinal instability, and neural compression [2]. For the remainder of patients, physicians use

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prognostic scores to identify the most suitable treatment method [3]. These prognostic scores are composed of different factors, each of which has a different significance. The modified Tokuhashi score [4], the Tomita score [2] and the Spine Instability Neoplastic score (SINS) [5] are currently widely used. However, the reliability of such prognostic scores has been difficult to prove, and researchers have failed to reach an agreement in previous studies [1,6-8]. Yamashita et al. [9] reported a prediction accuracy in 67 (79%) of 85 patients who were followed-up for 1 year or longer, and the modified Tokuhashi score was shown to be useful regardless of the selected treatment [9].

The decision for a surgical approach is still cataloged according to classifications that we believe are not relevant at the present time. Therefore, the present study has two main objectives. First, to assess the reliability of prognostic scores for patients who were treated surgically for symptomatic thoracolumbar spinal metastases in a retrospective single-center cohort. Second, to evaluate the impact of previous systemic treatments, such as immunotherapy and hormonotherapy, on overall survival.

Methods

This study retrospectively examined the clinical data of 60 adult patients at Centre Hospitalier Universitaire Vaudois (CHUV) who had been diagnosed with extradural thoracolumbar spinal metastases and who had undergone spinal surgery at the CHUV between January 2011 and December 2018. The exclusion criteria were intradural metastases, being a minor, refusal to participate and missing data. The study was reviewed by the regional ethics committee, which approved the analysis of data for all patients, including deceased and presumed deceased patients.

The following medical and imaging data were collected and used: sex, age, comorbidities, primary cancer, diagnosis and tumor biology, clinical symptoms, neurological exam, Karnofsky performance score (KPS) [10], previous treatment(s), current treatment, surgical intervention, imaging information, pain medication, morbidity, mortality, tumor recurrence, progression-free survival, prognostic scores (modified Tokuhashi score, Tomita score), and spine instability neoplastic score (SINS). Variables for which more than 50% of values were missing were excluded to prevent model distortion.

The patients (n = 60) were divided into two groups based on their Tokuhashi score. Group 1 (Tokuhashi score 0–8, n = 37) consisted of patients with short (<6 months) predicted survival times, and Group 2 (Tokuhashi score 9–15, n = 23) consisted of patients with long (>6 months) predicted survival times. The performance of the Tokuhashi score was estimated with a receiver operating characteristic (ROC) curve and the corresponding area under the curve (AUC). The median survival and probability of survival were determined by the Kaplan-Meier estimator and log-rank test to compare the survival between the two score-based patient groups. The significance of each variable for postoperative survival was determined with the Cox proportional hazards model.

To evaluate the influence of previous or ongoing immunotherapy and/or hormonotherapy on the outcome, a Kaplan-Meier analysis was used. The log-rank test determined if the presence of these treatment options had a statistical significance on the survival. A similar analysis was done, to identify the impact of the primary tumor type on the overall survival.

Results

The mean age of the patients was 64.20 ± 10.61 years (range 42–83). The mean survival of all 60 patients was 16.47 ± 23.07 months (range 1–114). The mean male (73.33% of the total cohort) survival time was 15.91 months, and the mean female (26.67%) survival duration was 16.00 months. The primary tumor types were lung (n = 22), prostate (n = 10), breast (n = 6), renal (n = 5), hepatic (n = 4), and others (n = 13). All patients were scored according to the KPS, SINS, modified Tokuhashi score, and Tomita score. Preoperative pain was noted for 53 patients (88.33%), and various degrees of neurologic deficit were noted for 34 patients (56.67%). Since chemotherapy and radiotherapy are standard treatments for metastatic patients, we were interested in patients who had benefitted from immunotherapy and/or hormonotherapy. There were 22 patients (36.67%) who had received immunotherapy and/or hormonotherapy. Most patients who were treated with hormonotherapy were those with primary tumors in prostate or breast tissue, since these tumors are the most sensitive to this kind of systemic therapy. Some patients suffered from organ insufficiencies: hepatic insufficiency was present in 17 patients (28.33%), and renal insufficiency was present in 10 patients (16.67%). Patient demographics are summarized in Table 1.

According to the modified Tokuhashi score, 37 of 60 patients (Group 1) had a Tokuhashi score in the range of 0–8, which corresponds to less than 6 months of survival, and 23 of 60 patients (Group 2) had a modified Tokuhashi score in the range of 9–15, which corresponds to more than 6 months of survival. However, the actual mean survival of Group 1 was 11.62 ± 16.49 months (range 1–71), and the actual mean survival of Group 2 was 24.26 ± 29.65 months (range 1–114). Overall, the Tokuhashi prediction score had an accuracy of 55%. For Group 1, the Tokuhashi score prediction was correct in 19 (51%) patients and incorrect in 18 (49%) patients. For Group 2, the modified Tokuhashi score prediction was correct in 14 (61%) patients and incorrect in 9 (39%) patients.

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Table 1: Patient demographics.

Variable	N	%
Sex		
Male	44	73.33
Female	16	26.67
Age		
<65 years	28	46.67
≥65 years	32	53.33
Tumor type		
Lung	22	36.67
Prostate	10	16.67
Breast	6	10.00
Liver	4	6.67
Kidney	5	8.33
Other	13	21.67
KPS		
0-40%	4	6.67
50-70%	26	43.33
80-100%	30	50.00
SINS		
7-12	47	78.33
13-18	13	21.67
Tokuhashi		
0-8	37	61.67
9-15	23	38.33
Tomita		
2-3	1	1.67
4-5	17	28.33
6-7	17	28.33
8-10	25	41.67
Pain	53	88.33
Neurologic deficit	34	56.67
Immuno/hormonotherapy	22	36.67
Hepatic insufficiency	17	28.33
Renal insufficiency	10	16.67

The ROC curve (Figure 1) for the performance of the modified Tokuhashi score had an AUC of 0.61. Because it is only slightly more accurate than a random classifier, the modified Tokuhashi score is not a useful prognostic score in a clinical setting. When one point was added to the score for every patient who received immunotherapy or hormonotherapy, no statistically significant difference to the modified Tokuhashi score was found.

Kaplan-Meier analysis (Figure 2) of the modified Tokuhashi score revealed differences between Group 1 and Group 2 in terms of survival. The log-rank test (Table 2) yielded a chi-square value of 5.428 and a *p* value of 0.020. This result indicated that the two score groups were significantly different in terms of survival. Another scoring system that exhibited a significant difference between groups was the Tomita score, with a chi-square value of 13.70 and a *p* value of 0.003. KPS and SINS were not statistically significant.

Univariate analysis (Table 3) was performed with Cox proportional hazard regression for each variable to determine the influence of each variable on survival. The chosen reference for the scoring systems and primary tumor type variables was the one with the best estimated survival. The variables that were statistically significant were pulmonary primary tumor (*p* value 0.023), modified Tokuhashi score (*p* value 0.021), Tomita score (*p* value between 0.392 and 0.002 depending on the obtained score), and preoperative pain (*p* value 0.002). Previous or ongoing immunotherapy and/or hormonotherapy did not have a statistically significant impact on survival according to the univariate analysis (*p* value 0.359). To

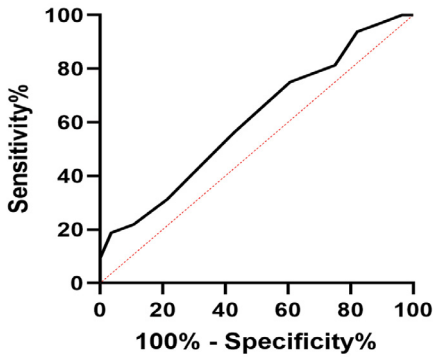

Figure 1: ROC curve of the modified Tokuhashi score for our complete cohort (60 patients).

Table 2: Log rank (Mantel-Cox) test for each scoring system.

Scoring system	Chi-square	df	P value
KPS	1.198	2	0.549
SINS	0.351	1	0.554
Modified Tokuhashi score	5.428	1	0.020
Tomita score	13.70	3	0.003

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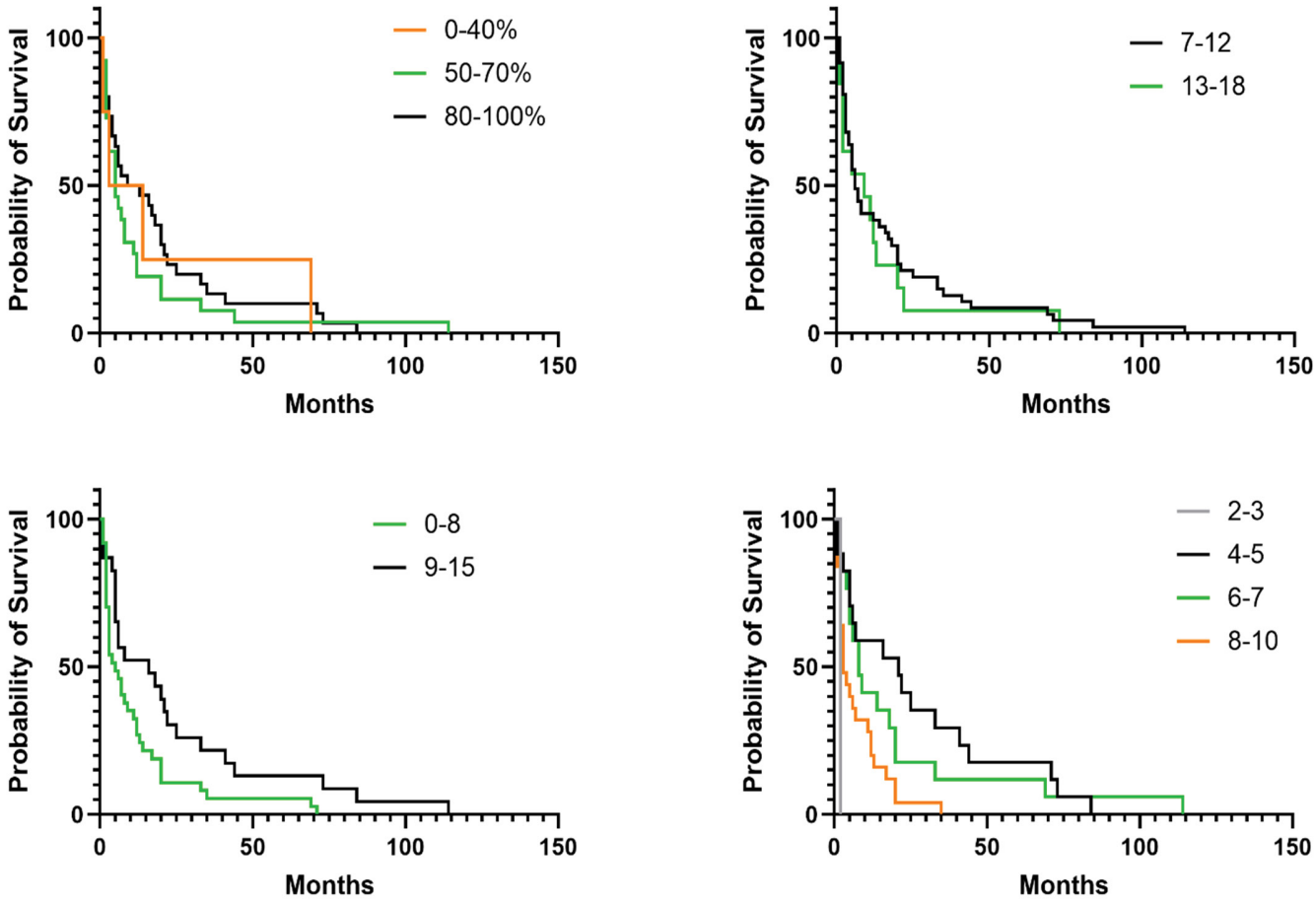

Figure 2: Kaplan-Meier curves for the KPS (a), SINS (b), modified Tokuhashi (c), and Tomita (d) scoring systems.

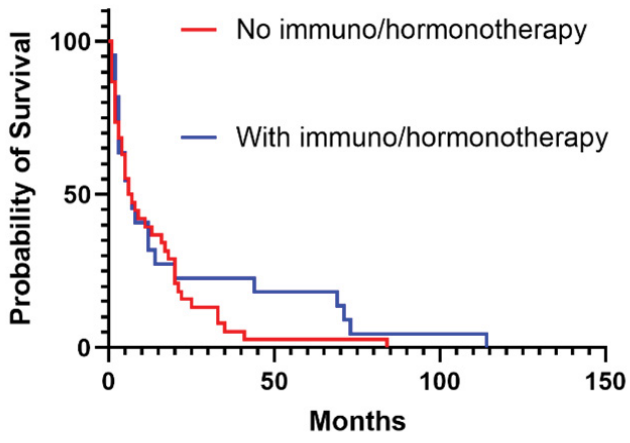

Figure 3: Kaplan-Meier curves showing differences in survival between patients who received immune/hormonotherapy and those who did not.

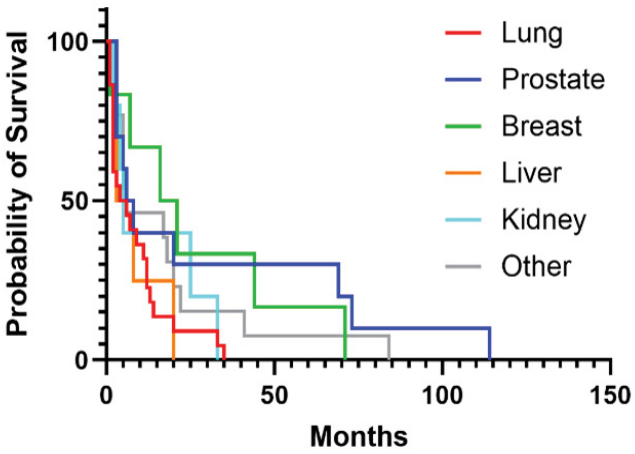

Figure 4: Kaplan-Meier curves showing the differences in survival for patients stratified by primary tumor type.

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further support this statement, another Kaplan-Meier curve analysis (Figure 3) with the corresponding log-rank test was performed with the following results: chi–square coefficient of 0.898 and *p* value of 0.343. There were no statistically significant differences between the groups who received immunotherapy and/or hormonotherapy and the groups who did not receive immunotherapy and/or hormonotherapy.

Survival depends on the primary tumor type, and patients with prostate or breast cancer have a greater chance of long-term survival (Figure 4). However, whether this is due to the increased use of other systemic therapies remains unclear.

Multivariate analysis (Table 3) revealed only two statistically significant variables, age (*p* value 0.002) and preoperative pain (*p* value 0.013), with no scoring system being statistically significant for survival outcome.

Discussion

In this study, we investigated whether the modified Tokuhashi score, which is widely used in contemporary clinical practice, is an adequate prognostic score for patients with spinal metastases. Although the accuracy of this scoring system is not particularly high, it was still shown to have some significance in the univariate analysis.

In this study, we demonstrate that the use of the modified Tokuhashi scale is not actually adapted for the decision-making process for patients with spinal metastatic lesions (given de AUC of 0.61). This is because treatment has radically changed, and the survival of these patients has significantly improved, especially with the use of hormone therapy and immunotherapy. In this study, we hypothesized that adding a point to the scale for patients who received immunotherapy/hormone therapy would improve the prognostic value of the Tokuashi scale. However, even though there is an improvement, it does not have a sufficient impact to be useful in the decision-making process. It is important to note that we must seek new ways to better predict the survival of these patients.

Spinal vertebral metastasis represents a critical and challenging aspect of oncological care, demanding nuanced surgical decision-making processes. Metastatic lesions involving the spine are frequently encountered in patients with advanced cancer and pose significant risks to neurological function, structural integrity, and overall quality of life.

The decision to pursue surgical intervention for spinal vertebral metastasis requires careful consideration of numerous factors, including the patient's overall health status, extent of spinal cord compression, presence of neurological deficits, tumor histology, prognosis, and the potential benefits and risks associated with surgery.

The primary goals of surgical intervention for treating spinal vertebral metastasis include alleviating pain, preserving or restoring neurological function, stabilizing spinal column integrity, and optimizing patient mobility and quality of life. However, the complex nature of metastatic spinal lesions necessitates an individualized approach tailored to each patient's unique circumstances.

Several studies have evaluated the reliability and predictive value of the modified Tokuhashi score in different patient populations. Overall, the score has shown moderate reliability in predicting survival outcomes for patients with spinal metastases. However, its accuracy may vary depending on factors such as the primary tumor type, patient demographics, and the presence of comorbidities [11].

One of the limitations of the modified Tokuhashi score is its reliance on subjective assessments of certain variables, such as the patient's general condition and neurological status. Additionally, the score may not fully capture the heterogeneity of spinal metastases and individual patient characteristics that can influence prognosis [12,13].

Predictive models such as the modified Tokuhashi score are based on statistical analysis of patient data and do not always accurately predict individual outcomes.

Furthermore, advances in imaging modalities, surgical techniques, and perioperative care have significantly enhanced the safety and efficacy of surgical interventions for treating spinal vertebral metastasis, improving patient outcomes and prolonging survival.

Despite these advances, the decision to perform surgery for spinal vertebral metastasis remains complex and must be approached with careful consideration of the risks, benefits, and patient preferences. Shared decision-making between patients, their families, and health care providers is essential in navigating the treatment landscape and aligning therapeutic goals with individual values and priorities.

Conclusion

Tokuashi scoring system is not reliable in assessing survival in patients spinal metastatic disease.

Surgical decision-making for patients with spinal vertebral metastasis represents a dynamic and evolving aspect of oncological practice, emphasizing the importance of personalized care, interdisciplinary collaboration, and informed patient-centered decision-making to optimize outcomes and enhance quality of life for patients facing this challenging condition.

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