

CORRELATION BETWEEN ACTUAL SURVIVAL AND TOKUHASHI AND TOMITA SCORES IN SPINE METASTASES

CORRELAÇÃO ENTRE A SOBREVIDA REAL E OS ESCORES DE TOKUHASHI E TOMITA EM METÁSTASES DE COLUNA VERTEBRAL

CORRELACIÓN ENTRE LA SUPERVIVENCIA REAL Y LAS PUNTUACIONES DE TOKUHASHI Y TOMITA EN LAS METÁSTASIS DE LA COLUMNA VERTEBRAL

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ABSTRACT

Objective: To evaluate the accuracy of the scores of Tokuhashi and Tomita and the actual survival of patients with vertebral metastases. **Methods:** A retrospective assessment of 45 patients with spinal metastases. Thirty-one patients underwent surgical treatment and adjuvant therapy and 14 received conservative treatment (chemotherapy/radiotherapy) or palliative/supportive, depending on the scores of Tokuhashi and Tomita. **Results:** In the study, 80% of patients were female and the mean age was 57.8 years (SD=11.3 years). The most frequent primary tumors were breast and prostate (68.9%). The accuracy of Tokuhashi scale was 53.4% and the Tomita, 64.5%. The concentration of Tomita range of correct classification was in the category of survival > 12 months (57.8%), while the Tokuhashi scale presented some adjustment in the other categories, < 6 months (15.6%) and 6 to 12 months (2.2%). The histological type of the primary tumor was the only variable that statistically influenced the survival time of patients ($p < 0.001$), and patients with lung or liver tumor (most aggressive) presented a risk of death 9.89 times higher than patients with primary tumors of breast or prostate (less aggressive) (95% CI: 3.10 to 31.57). **Conclusion:** The Tokuhashi and Tomita scores showed good accuracy with respect to the actual survival of patients with tumor metastasis in the spine.

Keywords: Spine; Neoplasms; Metastasis.

RESUMO

Objetivo: Avaliar a acurácia entre os escores de Tokuhashi e Tomita e a sobrevida real dos pacientes acometidos por metástase vertebral. **Métodos:** Foram avaliados retrospectivamente 45 pacientes com metástases vertebrais. Trinta e um pacientes foram submetidos a tratamento cirúrgico e a terapia adjuvante e 14 apenas receberam tratamento conservador (quimioterapia/radioterapia) ou paliativo/de suporte, dependendo da pontuação dos escores de Tokuhashi e Tomita. **Resultados:** No estudo, 80% dos pacientes eram do sexo feminino e a média de idade foi 57,8 anos (DP=11,3 anos). Os tumores primários mais encontrados foram de mama e próstata (68,9%). A acurácia da escala de Tokuhashi foi de 53,4% e a de Tomita, de 64,5%. A concentração dos acertos de classificação da escala de Tomita foi na categoria sobrevida > 12 meses (57,8%), enquanto a escala de Tokuhashi apresentou algum acerto nas demais categorias, < 6 meses (15,6%) e de 6 a 12 meses (2,2%). O tipo histológico do tumor primário foi a única variável que influenciou estatisticamente o tempo de sobrevida dos pacientes ($p < 0,001$), sendo que pacientes com tumor de pulmão ou fígado (mais agressivos) apresentaram risco de vida 9,89 vezes maior que os pacientes com tumor primário de mama ou próstata (menos agressivos) (IC 95%: 3,10 a 31,57). **Conclusão:** Os escores de Tokuhashi e de Tomita apresentaram boa acurácia com relação à sobrevida real dos pacientes acometidos por metástases na coluna vertebral.

Descritores: Coluna vertebral; Neoplasias; Metástase.

RESUMEN

Objetivo: Evaluar la exactitud de las puntuaciones de Tokuhashi y Tomita y la supervivencia real de pacientes con metástasis vertebrales. **Métodos:** Se evaluaron retrospectivamente 45 pacientes con metástasis vertebrales. Treinta y un pacientes fueron sometidos a tratamiento quirúrgico y terapia adyuvante y 14 recibieron sólo tratamiento conservador (quimioterapia/radioterapia) o paliativo/de apoyo, dependiendo de las puntuaciones de Tokuhashi y Tomita. **Resultados:** En el estudio, el 80% de los pacientes eran mujeres y edad media fue de 57,8 años (DE = 11,3 años). Los tumores primarios más frecuentes fueron mama y próstata (68,9%). La exactitud de la escala Tokuhashi fue de 53,4% y la de Tomita, de 64,5%. La concentración de aciertos de clasificación en la escala de Tomita fue en la categoría de supervivencia > 12 meses (57,8%), mientras que la escala Tokuhashi presentó algunos ajustes en las otras categorías < 6 meses (15,6%) y de 6 a 12 meses (2,2%). El tipo histológico del tumor primario fue la única variable que influyó estadísticamente el tiempo de supervivencia de los pacientes ($p < 0,001$), y los pacientes con tumor de pulmón o hígado (más agresivos) presentaron riesgo de vida 9,89 veces mayor que los pacientes con tumores primarios de mama o de próstata (menos agresivos) (IC del 95%: 3,10 a 31,57). **Conclusión:** Las puntuaciones de Tokuhashi y Tomita mostraron una buena precisión con respecto a la supervivencia real de pacientes con metástasis en la columna vertebral.

Descriptores: Columna vertebral; Neoplasias; Metástasis.

INTRODUCTION

The spine is the most common site of bone metastasis. Between 30% and 70% of cancer patients will have evidence of metastasis in the spine in post-mortem exams.¹

The most common tumors that metastasize to the spine are breast, lung, kidney, prostate, thyroid, melanoma, lymphoma, and colorectal. Most metastases occur in the thoracic spine (70%), followed by the lumbar spine (20%) and the cervical spine (10%). Multiple

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non-contiguous metastases are found in 10% to 38% of cases.¹

Spinal metastases can cause significant clinical problems for patients, including pain and neurological symptoms. Pain can be a direct effect, caused by a local or indirect inflammatory response, or due to instability and/or a fracture caused by the actual metastasis. Similarly, the neurological symptoms of medullary or radicular compression are caused directly by the tumor mass, or indirectly by the fracture or deformity resulting from the instability. Around 10% of patients with some type of tumor develop neurological compression due to metastases to the spine.²

The incidence of metastases to the spine is increasing. Factors such as population aging and improvements in medical treatment for cancer, which increase patient survival time, are contributing to the development of metastatic disease in higher numbers of patients.³

With advances in chemotherapy, radiation therapy, and hormone therapy, the life expectancy of patients has increased. Progress has been made in surgical techniques, together with advances in technology, enabling more effective surgical treatment of spinal metastases.⁴

The role of the surgeon in metastatic tumors of the spine is always a subject of discussion, because the surgeon can improve mechanical instability, medullary compression, and pain, but there are still doubts as to the surgeon's role in increasing survival times. In the past, decompression techniques without stabilization resulted in worse outcomes than radiation therapy. Thus, one might think that radiation therapy is the preferred option when compared to surgery for certain types of cancers. However, recent evidence has shown that modern surgery (including anterior and posterior approaches with stabilization) generates better results than isolated radiation therapy, and that the quality of life of those patients also increases.^{5,6}

When opting for surgical treatment, we must keep in mind that in most patients with metastatic spinal tumors, life expectancy governed by the site of the primary tumor and by staging, generally around 1 to 2 years of survival time, since tumor metastasis in and of itself indicates an already advanced stage of the disease. Therefore, surgery should not have a negative impact on the remaining quality of life. The rate of surgical complications can be high (20-30%) and this should be taken into account in selecting the treatment. This is especially applicable in complex surgeries such as en bloc resections, which are associated with an increase in morbidity and mortality as compared to simpler procedures, such as palliative resections. Although surgery is currently considered the treatment of choice for spinal metastases, more evidence is necessary to define the role and the indications of the various surgical techniques and the newer, more radical treatments available.²

Several survival scoring systems have been developed, among them those proposed by Tokuhashi *et al.*^{7,8} and by Tomita *et al.*⁹ These scores are tools used to help choose the best treatment for patients with spinal metastases, based on average survival time.

The objective of this study was to evaluate the accuracy between the Tokuhashi and Tomita scores and the actual survival time in patients with spinal metastases.

MATERIALS AND METHODS

Following approval by the Ethics Committee of the Universidade Estadual de Campinas (UNICAMP), Campinas, SP, Brazil, 45 patients with metastases to the spine, who were in follow-up at the Spinal Surgery Clinic of the Department of Orthopedics at UNICAMP, were evaluated retrospectively. Of these 45 patients, 31 had undergone surgery and adjuvant chemotherapy and/or radiation therapy and 14 had received only adjuvant (chemotherapy and/or radiation therapy) or palliative/supporting treatment, in accordance with the Tokuhashi and Tomita scores.

Patients with metastasis to the spine who were evaluated by radiographs, axial computed tomography, and magnetic resonance of the entire spine, as well as bone scintigraphy, and magnetic resonance of the chest, abdomen, and skull, were included in this study. These exams were standardized in order to diagnose and

stage the patients. Patients with incomplete medical records, and in whom the Tokuhashi and Tomita scores had not been calculated, were excluded. The minimum follow-up time was one year.

The Tokuhashi score was developed to indicate the type of treatment in metastatic lesions of the spine, based on the following criteria: 1) General condition of the patient, according to Karnofsky and Young¹⁰: poor, 0 points; moderate, 1 point; and good, 2 points; 2) Number of extraspinal metastases: greater than or equal to three, 0 points; two, 1 point; and one, 2 points; 3) Number of spinal metastases: greater than or equal to three, 0 points; two, 1 point; and one, 2 points; 4) Resectability of metastases in vital organs: non-resectable, 0 points; resectable, 1 point; and absent, 2 points; 5) Site of the primary tumor: lung and stomach, 0 points; kidney, liver, and uterus, 1 point; and thyroid, prostate, breast, rectum, others, and unidentified, 2 points; 6) Medullary neurological compromise: total, 0 points; incomplete, 1 point; absent, 2 points. A score of from 0 to 2 is given for each of the six parameters for a maximum of 12 points.⁷ The authors later modified the scoring system, changing the site of the primary tumor parameter, which now ranges from 0 to 5 points, due to its relevance in the prognosis of these patients.⁸

After this modification, the new score was: lung, osteosarcoma (which was included in the list, despite being a primary bone tumor), stomach, bladder, esophagus, and pancreas, 0 points; liver, ureter, and unidentified, 1 point; other, 2 points; kidney and uterus, 3 points; rectum, 4 points; and thyroid, breast, prostate, and carcinoid, 5 points. In this study, the revised Tokuhashi score was used. (Table 1)

Based on these indices, Tokuhashi *et al.*⁸ define the prognosis and the treatment option for these patients, respectively, as follows: a) 0 to 8 points, prognosis of up to 6 months, conservative or palliative treatment in isolated cases; 9 to 11 points, prognosis greater than 6 months, palliative treatment or excisional surgery in cases of a single lesion and without metastases to vital organs; 12 to 15 points, prognosis of more than 1 year, treatment with excisional surgery. (Table 2)

Table 1. Scale of Tokuhashi *et al.*

Characteristic	Points
1 - General condition (performance status)	
Poor (PS 10%-40%)	0
Moderate (PS 50%-70%)	1
Good (PS 80%-100%)	2
2 - Extraspinal Metastases	
≥ 3	0
1-2	1
0	2
3 - Spinal Metastases	
≥ 3	0
1-2	1
0	2
4 - Visceral Metastases	
Not removable	0
Removable	1
none	2
5 - Primary site	
Lung, osteosarcoma, stomach, bladder, esophagus, and pancreas	0
Liver, bile duct, unknown	1
Others	2
Kidney, ureter	3
Rectum	4
Thyroid, breast, prostate, carcinoid tumor	5

The scoring system of Tomita *et al*⁹ assigns points based on three prognostic factors: 1) Degree of malignancy of primary tumor in terms of growth (slow, 1 point; moderate, 2 points; and rapid, 4 points); 2) Presence of visceral metastasis (without metastasis, 0 points; treatable, 1 point; untreatable, 4 points); and 3) Presence of bone metastasis (solitary or isolated, 1 point; multiple, 2 points). The total may range from 2 to 10 points. (Table 3)

According to Tomita *et al*⁹, the treatment strategy will be: a) 2 to 3 points, wide or marginal excision for long term local control; b) 4 to 5 points, marginal or intralesional excision for midterm local control; c) 6 to 7 points, palliative surgery for short term control; d) 8 to 10 points, non-surgical treatment. (Table 4)

In the study of Tomita *et al*⁹, patients with scores of 2 or 3 have an average survival time of 38.2 months, scores of 4 or 5 have an average survival time of 21.5 months, 6 and 7 points a survival time of 10.1 months, and patients with a score of 8 to 10 points have an average survival time of 5.3 months. Therefore, to standardize the Tomita scale in relation to the Tokuhashi scale, patients with total points of between 2 and 5 have an average survival time of more than 12 months; those with 6 or 7 points have an average survival time of 6 to 12 months; and those with a total of between 8 and 10 points have a survival time of less than 6 months.

The patients were categorized into three groups according to score: Tokuhashi 0-8 points (Group 1), 9-11 points (Group 2), and 12-15 points (Group 3), Tomita 8-10 points (Group 1), 6-7 points

Table 2. Prognosis and treatment according to Tokuhashi *et al*.

Result	Prognosis	Treatment
0 to 8 points	6 months	Conservative
9 to 11 points	6-12 months	Palliative or Excisional
12 to 15 points	More than 12 months	Excisional

Table 3. Scale of Tomita *et al*.

	Score
Degree of malignancy	
Slow	1
Moderate	2
Rapid	4
Visceral Metastasis	
Absent	0
Treatable	2
Untreatable	4
Bone Metastasis	
Solitary	1
Multiple	2

Table 4. Prognosis and treatment according to the scale of Tomita *et al*.

Result	Treatment Strategy
2-3 points	Wide or marginal excision, long term control.
4-5 points	Marginal or intra-lesion excision, medium term control.
6-7 points	Palliative surgery, short term control.
8-10 points	Non-surgical treatment.

(Group 2), and 2-5 points (Group 3). Similarly, the patients were categorized by actual survival time into three groups: survival < 6 months (Group 1), 6-12 months (Group 2), and survival > 12 months (Group 3). Thus, we evaluated the agreement of the Tokuhashi and Tomita scores categorized into groups, with the group in which the actual survival time was categorized.

RESULTS

Forty-five patients with metastatic disease in the spine were selected. The patients were classified into three groups using the Tokuhashi and Tomita scales: Group 1 (< 6 months of survival), Group 2 (6 to 12 months of survival), and Group 3 (> 12 months of survival), and were followed up to evaluate their actual survival times. Thus, it was possible to verify whether the scales developed by Tokuhashi *et al*⁸ and by Tomita *et al*⁹ were accurate in terms of the patients' actual survival times, and whether patient characteristics such as sex, age, site of the primary tumor, and surgery influenced the survival of patients with metastatic tumors of the spine.

The personal and diagnostic characteristics were described using summary measurements (average, standard deviation) by age and absolute and relative frequencies for sex, histological type of primary tumor, and surgical or non-surgical treatment. Nine patients presented neurological deficits, four of them with metastasis of breast cancer (Frankel D); one with epidermoid carcinoma of the uterus (Frankel D), one with prostate carcinoma (Frankel C); one with gastric carcinoma (Frankel C), and two with lung carcinoma (Frankel B).

The accuracies of the respective scales with the real survival groups were calculated, with confidence intervals of 95%.

The average survival time of the patients was estimated using the Kaplan-Meier function¹¹, by sex, age range, site of the primary tumor, and surgical or non-surgical treatment. Comparing the categories using the log-rank test,¹¹ the average survival time was calculated, as it was impossible to calculate the mean survival time due to the low number of deaths in certain categories. The Hazard Ratio (HR) was estimated using Cox's bivariate regression model, with the respective confidence intervals of 95%, and the risk of death among the categories was estimated using Cox's multivariate regression.

The tests were conducted with a level of significance of 5%.

Table 5 shows that most of the patients in the study were female (80%), with an average age of 57.8 years (SD = 11.3 years), and the primary tumors were divided according to aggressiveness. The least aggressive (breast and prostate) corresponded to 68.9%, the most aggressive (lung and liver) to 13.3%, and the other tumors to 17.8% of the patients selected. Approximately 69% of the patients underwent surgery.

Table 6 shows that the accuracy of the Tokuhashi scale was 53.4% and that of the Tomita scale was 64.5%, indicating slightly better accuracy for the Tomita scale than for the Tokuhashi scale.

Table 5. Description of the study patient characteristics.

Variable	Description (N = 45)
Sex, n (%)	
Female	36 (80)
Male	9 (20)
Age (years)	
Average (SD)	57.8 (11.3)
Primary tumor, n (%)	
Breast + Prostate	31 (68.9)
Lung + Liver	6 (13.3)
Others	8 (17.8)
Surgery, n (%)	
No	14 (31.1)
Yes	31 (68.9)

Table 6. Description of real survival of the patients according to the scales and the accuracy results of the scales.

Scales	Survival								Accuracy (CI 95%)
	< 6 months		6 to 12 months		> 12 months		Total		
	n	%	n	%	n	%	n	%	
Tokuhashi									53,4 (38,8; 68,0)
< 6 months	7	15.6	1	2.2	5	11.1	13	28.9	
6 to 12 months	3	6.7	1	2.2	9	20.0	13	28.9	
> 12 months	0	0.0	3	6.7	16	35.6	19	42.2	
Tomita									64.5 (50.5; 78.5)
< 6 months	3	6.7	0	0.0	1	2.2	4	8.9	
6 to 12 months	0	0.0	0	0.0	3	6.7	3	6.7	
> 12 months	7	15.6	5	11.1	26	57.8	38	84.4	
Total	10	22.2	5	11.1	30	66.7	45	100	

The concentration of matches with the Tomita scale was in the survival > 12 months category (57.8%), while the Tokuhashi scale presented some matches in the other categories - < 6 months (15.6%) and 6 to 12 months (2.2%).

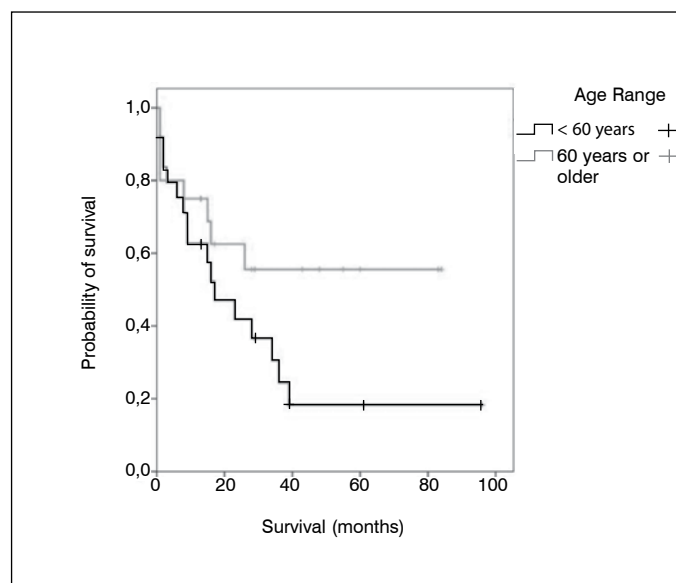
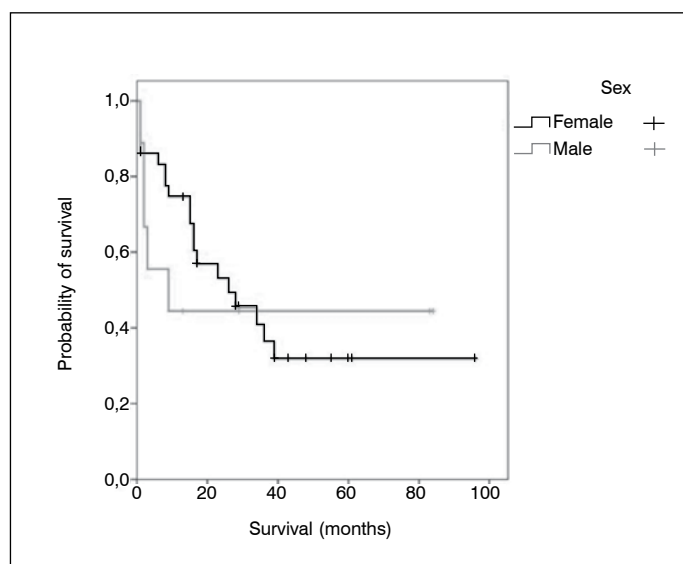
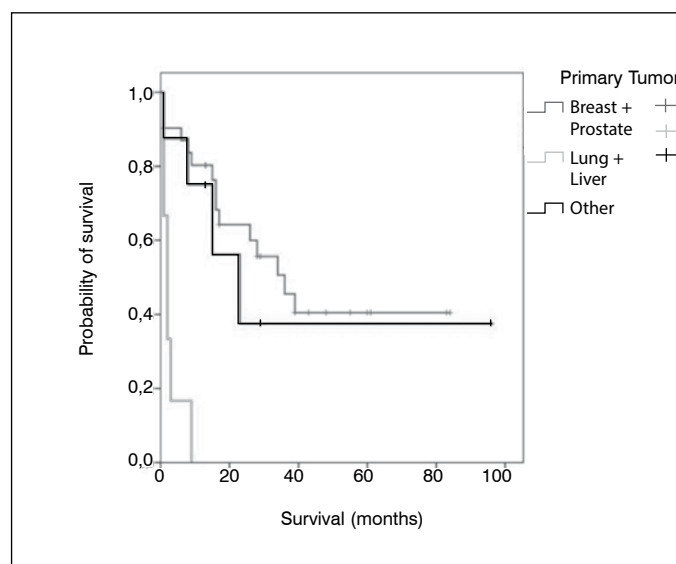
Figures 1-4 suggest that the histological type of the primary tumor (breast and prostate) was the only variable among those evaluated that influenced patient survival.

Table 7 shows that the histological type of the primary tumor was the only variable that influenced the survival time of the patients statistically ($p < 0.001$), and that patients with lung or liver tumors (more aggressive) had a 9.89 times greater risk of death than patients with breast or prostate (less aggressive) primary tumors (CI95% : 3.10 to 31.57).

DISCUSSION

The spine is the most common site of tumor metastasis to the bones. The incidence of metastases is increasing due to a population aging, an increase in life expectancy, and improvements in medical treatment of the primary tumors due to the use of chemotherapy, radiation therapy, and hormone therapy.¹²⁻¹⁴

The tumors that most commonly metastasize to the spine are those of the breast, lung, kidney, prostate, thyroid, melanoma, lymphoma,

**Figure 2.** Kaplan-Meier function of patient survival by age range.**Figure 1.** Kaplan-Meier function of patient survival by sex.**Figure 3.** Kaplan-Meier function of patient survival by primary tumor.

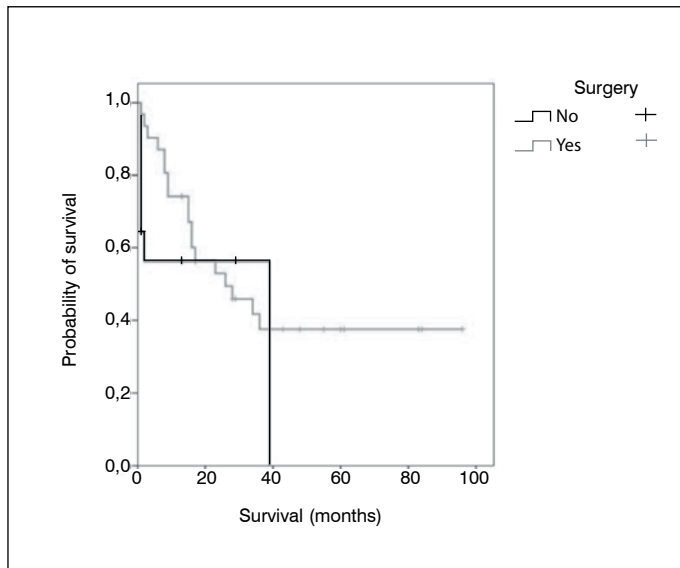


Figure 4. Kaplan-Meier function of patient survival by surgical status.

and colorectal.¹⁵⁻¹⁷ The presence of bone metastases to the spine often indicates that the disease at the primary site is incurable; however, with better adjuvant therapies, patients with metastases are living for longer periods following diagnosis.¹⁸

Some prognostic classifications are used to guide the treatment of patients affected by metastatic disease of the spine in terms of the best therapeutic option. Among them we cite Tokuhashi *et al.*,^{7,8} Sioutos *et al.*,¹⁹ Van der Linden *et al.*,²⁰ Tomita *et al.*,⁹ and Bauer *et al.*^{21,22} In this study, the modified classification developed by Tokuhashi *et al.*⁸ and the classification developed by Tomita *et al.*⁹ were used.

Tokuhashi *et al.*⁸ described a prognostic evaluation system for metastatic tumors of the spine based on six variables: site of the primary tumor, presence or absence of paralysis, Karnofsky clinical performance status, number of extraspinal bone metastases, number of spinal metastases, and number of visceral metastases.

These six factors are evaluated together, producing a value ranging from 0 to 15 points, with zero indicating a poor prognosis and

15 a good prognosis (Table 2). It is interesting to note that Tokuhashi *et al.*⁸ consider neurological deficit to be a significant prognostic factor of survival.

Tomita *et al.*⁹ studied several prognostic factors for tumor metastases in order to describe a system based on three factors: the growth rate of the primary tumor, the number of bone metastases, and the number of visceral metastases. (Table 3)

These three factors are evaluated together, generating a score value from 2 to 10 points for a good to a bad prognosis, respectively. (Table 4)

The site of the primary tumor is considered to be the most important prognostic factor in both the Tomita and Tokuhashi scales. According to Tomita *et al.*⁹, metastases of breast, prostate, and thyroid cancers permit longer survival. According to the modified Tokuhashi scale, less aggressive tumors such as those of the breast, prostate, thyroid, and carcinoid tumors score 5 points. More aggressive tumors, like those of the lung, osteosarcoma, esophagus, and pancreas, score zero points, indicating a worse prognosis for patient survival.⁸

This study corroborates this information, given that the patients with breast or prostate metastases, considered a less aggressive histological type, survived longer than those with more aggressive tumors, such as tumors of the lung and liver. (Table 7 and Figure 3)

In another study, Enkaoua *et al.*²³ report that patients with spinal metastasis in which the site of origin of the primary tumor is unknown have a worse prognosis for survival. They also state that neurological deficit should not be considered a prognostic factor of survival because it can be resolved with decompression, and is related to the speed of growth of the tumor. However, Tokuhashi *et al.*⁸ consider neurological deficit to be an isolated prognostic factor to be considered, and it is therefore attributed a score in the evaluation scale described by those authors.

In our evaluation, nine patients had neurological deficits, four of them from metastasis of breast cancer (Frankel D), one from epidermoid carcinoma of the uterus (Frankel D), one from prostate carcinoma (Frankel C), one from gastric carcinoma (Frankel C), and two from carcinoma of the lung (Frankel B). The patients with metastasis from adenocarcinoma of the lungs died prior to any neurological recovery. The other patients recovered from the neurological deficit.

Zou *et al.*²⁴ report a differentiation in relation to the analysis of the Tomita and Tokuhashi scores. According to this study, the score

Table 7. Estimates of average survival times of the patients by characteristics of interest and comparative test results.

Variable	Average estimated time (months)	CI (95%)		HR	CI (95%)		Deaths	Total	%	p
		Lower	Higher		Lower	Higher				
Sex										0.699
Female	42.28	28.15	56.42	1.00			20	36	55.6	
Male	39.22	13.02	65.43	1.21	0.45	3.23	5	9	55.6	
Age range										0.104
< 60 years	31.10	16.58	45.61	1.00			17	25	68.0	
60 years or older	51.01	33.59	68.43	0.51	0.22	1.19	8	20	40.0	
Primary Tumor										<0.001
Breast + Prostate	45.27	32.14	58.40	1.00			15	31	48.4	
Lung + Liver	3.00	0.57	5.43	9.89	3.10	31.57	6	6	100.0	
Others	44.25	11.70	76.80	1.39	0.46	4.22	4	8	50.0	
Surgery										0.250
No	22.46	11.66	33.25	1.00			7	14	50.0	
Yes	45.99	31.38	60.60	0.60	0.25	1.48	18	31	58.1	
Total	42.38	29.37	55.38				25	45	55.6	

of Tokuhashi *et al*^{7,8} is better correlated with the analysis of short term survival, while that of Tomita *et al*⁹ is better correlated with long term survival.

This information corroborates with our findings, as we observed that the concentration of matches with the Tomita scale was in the > 12 months long-term survival category (57.8%), while the Tokuhashi scale had some matches in the other categories, < 6 months (15.6%) and from 6 to 12 months (2.2%) i.e. the short term and medium term categories, respectively.

In view of the doubts in relation to the survival of patients with metastases to the spine, an indication for a surgical or palliative approach for this group of patients is always a topic of discussion for the specialists, who need to recommend the best treatment. Control of the symptoms and a satisfactory level of function allow the patient

to go home, and minimize the costs and physical and psychological stress associated with hospitalization. Moreover, surgical intervention poses risks, and predicting how patients will evolve following surgery is the first step to selecting the best treatment.

CONCLUSION

The Tokuhashi and Tomita scores presented good accuracy compared with the real survival times of patients with tumor metastasis to the spine.

All authors declare no potential conflict of interest concerning this article.

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