

Predictors of survival in surgically treated patients of spinal metastasis

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ABSTRACT

Background: The spinal metastasis occurs in up to 40% of cancer patient. We compared the Tokuhashi and Tomita scoring systems, two commonly used scoring systems for prognosis in spinal metastases. We also assessed the different variables separately with respect to their value in predicting postsurgical life expectancy. Finally, we suggest criteria for selecting patients for surgery based on the postoperative survival pattern.

Materials and Methods: We retrospectively analyzed 102 patients who had been operated for metastatic disease of the spine. Predictive scoring was done according to the scoring systems proposed by Tokuhashi and Tomita. Overall survival was assessed using Kaplan–Meier survival analysis. Using the log rank test and Cox regression model we assessed the value of the individual components of each scoring system for predicting survival in these patients.

Result: The factors that were most significantly associated with survival were the general condition score (Karnofsky Performance Scale) ($P=.000$, log rank test), metastasis to internal organs ($P=.0002$ log rank test), and number of extraspinal bone metastases ($P=.0058$). Type of primary tumor was not found to be significantly associated with survival according to the revised Tokuhashi scoring system ($P=.9131$, log rank test). Stepwise logistic regression revealed that the Tomita score correlated more closely with survival than the Tokuhashi score.

Conclusion: The patient's performance status, extent of visceral metastasis, and extent of bone metastases are significant predictors of survival in patients with metastatic disease. Both revised Tokuhashi and Tomita scores were significantly correlated with survival. A revised Tokuhashi score of 7 or more and a Tomita score of 6 or less indicated >50% chance of surviving 6 months postoperatively. We recommend that the Tomita score be used for prognostication in patients who are contemplating surgery, as it is simpler to score and has a higher strength of correlation with survival than the Tokuhashi score.

Key words: Spine metastasis, prognostic predictors, survival

INTRODUCTION

The skeletal metastasis in spine occurs in up to 40% of cancer patients.^{1,2} Surgery is indicated for radio-resistant tumors (e.g., sarcomas and lung, colon and renal cell carcinomas), spinal instability, neural compression, deformity, intractable pain, and failure of radiotherapy and for relief of symptoms.³⁻⁶ Only those patients who have a

reasonable life expectancy after surgery should be exposed to the morbidity associated with surgery. Prediction of life expectancy is difficult due to the diverse range of factors that determine survival in patients with malignancies.⁷⁻¹¹ Our study aimed to assess certain variables in patients with spinal metastases requiring surgery with regard to their value in predicting postsurgical life-expectancy. We also compared the revised Tokuhashi and the Tomita scoring systems, two commonly used prognostic scoring systems for spinal metastases and to suggest criteria for selecting patients for surgery based on the postoperative survival pattern.

MATERIALS AND METHODS

We retrospectively analyzed the data of 102 patients who underwent surgery for metastatic spine disease at our institute. There were 54 females (53%) and 48 males (47%). The median age at presentation was 58.5 years. The most common presenting symptoms for patients with spinal metastasis were pain and weakness [Figure 1]. The commonest malignancy was breast cancer ($n=25$, 24.51%), followed by lung cancer ($n=16$, 15.69%).

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The indications for surgery included radiological cord compression, impending neurological problem, impending pathological fracture, and intractable pain. Posterior surgery was performed in morbid and high-risk patients. Conservative decompression laminectomy was performed if the spine was deemed stable, for example, when the thoracic spine was affected and there was involvement of less than 50% of the vertebral body. Instrumentation was added when the fracture was deemed unstable and in need of supplementation. Anterior surgery was chosen for the relatively less morbid and low-risk patients.

All the patients were operated at the same institution by a group of four fellowship-trained spine surgeons. Oncology physicians were also involved in the treatment for chemotherapy or radiotherapy, when indicated. All the patients in the study were followed up postoperatively up to death.

Mortality records were retrieved from the National Cancer Registry. Predictive scoring was done based on the scoring systems proposed by Tokuhashi *et al.*¹² and Tomita *et al.*¹³ The prognostic values of the Tokuhashi and Tomita scores for predicting 6 month postoperative survival were compared. We also analyzed the effect of the time lapse between diagnosis of primary cancer and presentation of spinal secondary on postoperative life expectancy. Overall survival was analyzed using the Kaplan–Meier method. Individual components of each score were also assessed for significance as prognostic indicators using the log rank test and Cox regression model.

The revised Tokuhashi *et al.*¹² scoring system takes into account those parameters that are expected to be significant in influencing the surgical outcome in patients with spinal metastases. These parameters include the Karnofsky Performance Scale (KPS), presence of extraspinal bone metastasis, number of vertebral levels involved, extension of metastasis to an internal organ, presence of spinal cord palsy, and type of primary tumor. Tomita *et al.*¹³ used three factors proven to be significant for prognostication, namely,

the grade of malignancy, presence of visceral metastases, and presence of bone metastases. For both scoring systems, each parameter was assigned a weighted score and the total score was obtained by adding the scores of each component.

RESULTS

The thoracic spine was the most common site of involvement in our series of patients [Figure 2].

Univariate analysis

Gender: The median survival time for males was 5 months and for female it was 9 months (95% CI: 1 to 9) ($P < .05$, log rank test).

Age: Patients aged 55 years and below had a median survival of 12 months and those aged above 55 years had a median survival of 9 months ($P = .719$, log rank test). There was a trend for longer survival in younger patients.

Time to presentation with spinal metastasis: The spinal metastasis was the first indication of the presence of malignant disease in 29 patients. The median postoperative survival in these patients was 4 months (95% CI: 0 to 8.6), while those with known history of cancer and presenting with symptoms of spinal metastasis lived a median period of 7 months (95% CI: 4.23 to 9.77) post surgery. The difference was not statistically significant ($P = .296$, log rank test).

Analysis of individual components of the revised Tokuhashi scoring system

The most significant factors associated with survival were the general condition score (KPS) ($P = .000$, log rank test), extent of metastasis to internal organs ($P = .0002$, log rank test), and number of extraspinal bone metastases ($P = .0058$, log rank test) [Table 1].

The type of primary cancer did not influence the postsurgical survival according to the revised Tokuhashi scoring system ($P = .9131$). However, applying the scoring system originally

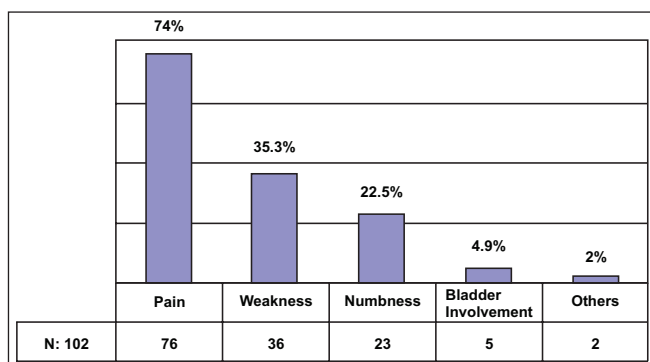


Figure 1: Bar diagram showing presenting symptoms

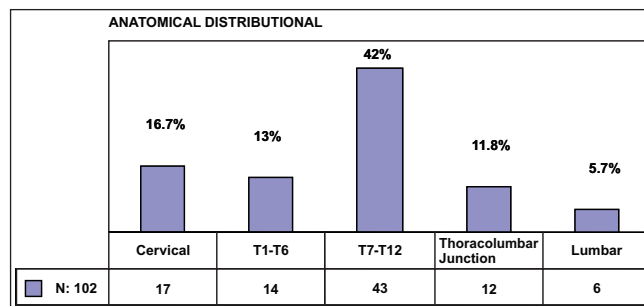


Figure 2: Bar diagram showing distribution of secondaries in the spine

proposed by Tokuhashi *et al.*,^{17,14} we found significant correlation between the score and survival ($P=.0027$, log rank test) [Table 2 and Figure 3].

Analysis of the Tomita *et al.* scoring system

The Tomita score had significant correlation with survival in our series of patients. All three components of the Tomita scoring system were found to have significant influence on survival [Table 3].

Multivariate analysis

We used the Wald (forward stepwise) method to rank the different parameters in the revised Tokuhashi and the Tomita scoring systems to evaluate which correlates most closely with survival. This showed that Tokuhashi ‘general condition,’ Tokuhashi ‘metastasis to internal organs,’ and Tokuhashi (old) ‘type of primary’ were the most accurate predictors of survival ($P=.000$, $P=.002$, and $P=.001$, respectively; chi-square test). Cross tabulation used to correlate strength of equivalent parameters in Tomita scoring system. It had shown that, visceral metastasis and

tumor activity in Tomita scoring system closely correlate with Tokuhashi metastasis to internal organ and older Tokuhashi primary tumor type respectively. There was significant correlation between these parameters (Spearman’s ratio: -1.000) [Figure 4].

To summarize, the parameters that influenced survival were: Tokuhashi general condition, Tokuhashi metastasis to internal organs, Tokuhashi (old) type of primary cancer, Tomita visceral metastasis, Tomita tumor activity

Parameters that not influenced survivals: Age, sex, Tokuhashi (revised) type of primary tumor, spinal cord palsy, Tokuhashi vertebral metastasis, Tokuhashi bone metastasis, Tomita bone metastasis

Six-month survival

The total Tokuhashi score can range from 0–15. We grouped the scores in our study into five groups and examined the likelihood of 6-month survival in each group [Table 4].

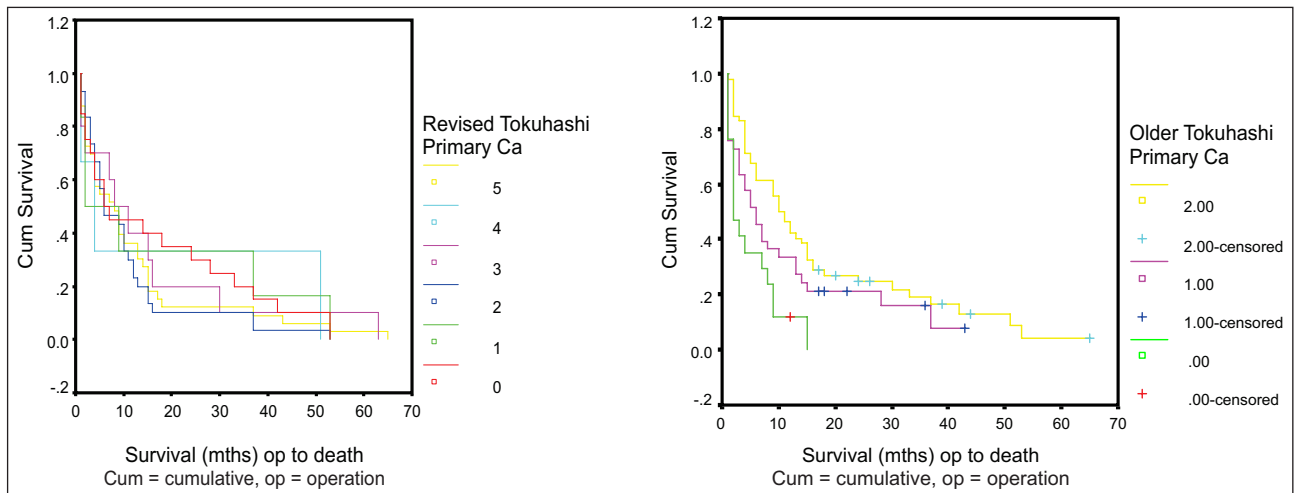


Figure 3: Survival function according to old and new Tokuhashi scoring systems

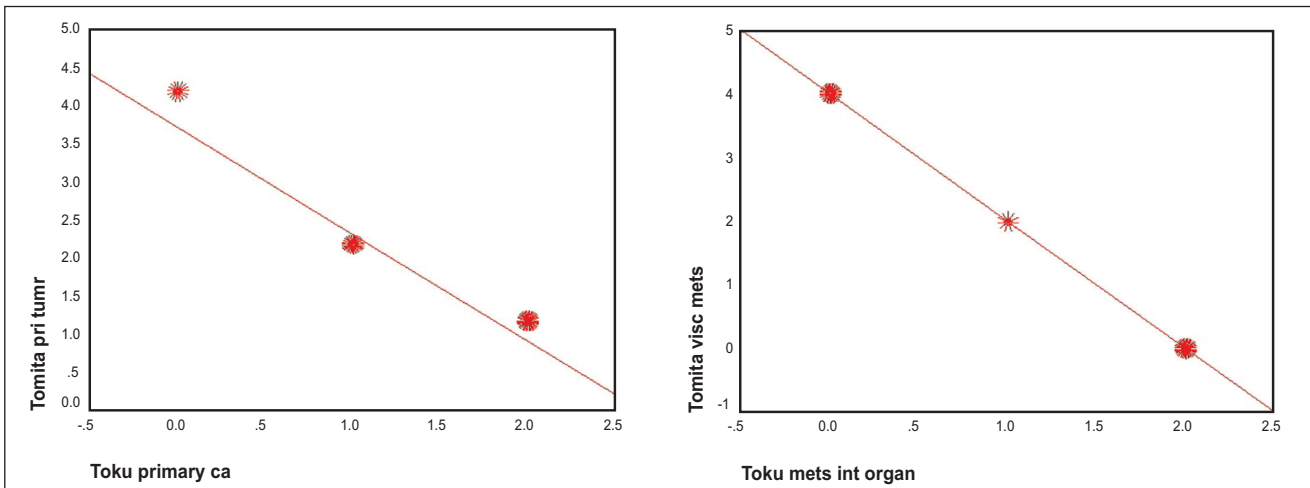


Figure 4: Cross-tabulation of Tomita and Tokuhashi metastasis

Table 1: Median survival for metastatic spine tumours (each Tokuhashi component)

Parameters	Log rank test	Score	No. of patients	Median survival (months)	95% CI (months)	
					Lower	Upper
Karnofsky performance scale	P=.0000	Poor (PS 10%–40%)	7	2	1	3
		Moderate (PS 50%–70%)	49	4	2	6
		PS 80%–100%	46	13	10	16
Extraspinal bone metastasis	P=.0058	More than 3 sites	17	3	1	5
		1–2 sites	45	7	3	11
		No extraspinal metastasis	40	12	6	18
Number of vertebral levels involved	P=.0763	Three or more vertebral levels	40	5	3	7
		Two levels	30	7	0	14
		Single level	32	10	3	17
Metastasis to internal organ	P=.0002	Non-removable	48	3	1	5
		Removable metastasis	11	7	4	10
		No metastasis	43	14	11	17
Presence of spinal cord palsy	P=.115	Frankel A, B	4	3	0	6
		Frankel C, D	90	7	5	9
		Frankel E, F	8	15	4	26
Type of primary tumor	P=.9131	Lung, osteosarcoma, stomach, bladder, esophagus, pancreas	20 (19.6%)	6	2	10
		Liver, gallbladder, unidentified	6 (5.9%)	2	0	8
		Others	30 (29.4%)	6	1	11
		Kidney, uterus	10 (9.8%)	8	2	24
		Rectum	3 (2.9%)	4	0	9
		Thyroid, breast, prostate, carcinoid tumor	33 (32.4%)	8	3	33

PS = Performance status

Table 2: Median survival for primary cancer against the original Tokuhashi scoring

Type of primary cancer	Log rank test	Score	n	Median survival (months)	95% CI (months)	
					Lower	Upper
Type of primary cancer	P=.0027	Lung, osteosarcoma, stomach, bladder, esophagus, pancreas	19	2	0.6	3
		Liver, gallbladder, unidentified	30	6	3	8.8
		Others	54	10	7	13

Table 3: Influence of individual components of the Tomita score on survival

Tomita <i>et al.</i>	Log rank test	Score	Patient	Median survival (Months)	95% CI	
Bone metastasis	P=.0450	Solitary	17	16	11	21
		Multiple	81	6	3	9
Visceral metastasis	P=.0003	No	41	14	11	17
		Treatable	11	7	4	10
		Untreatable	46	4	2	6
Tumor activity	P=.0030	Slow growth	51	10	7	13
		Moderate growth	30	6	3	9
		Rapid growth	17	2	1	3

There is significant difference in survival among the five Tokuhashi score groups ($P=.0038$, log rank test), with higher median survival in the groups with higher scores. The median survival time (and the 95% CI) are summarized in the following tables.

The 6-month survival rate was 55.1% for the group with

score 7–9, 63.2% for those with score 10–12, and 100% for those with score 13–15; these differences were statistically significant ($P<.05$, log rank test).

There is significant difference in survival between the four Tomita score groups ($P<.00005$, log rank test). Lower scores were correlated with higher median survival [Table 5].

Table 4: Revised Tokuhashi scores and the likelihood of 6-month survival

Revised Tokuhashi score groups	Median survival time	95% CI	Survival (months) surgery to death	
			<6 months	>6 months
0-3	1		Not computable due to small sample size	
4-6	4	1-7	13 (59.1)	9 (40.9)
7-9	7	4-10	22 (44.9)	27 (55.1)
10-12	13	4-22	7 (36.8)	12 (63.2)
13-15	15	10-20	0	8 (100)

Figures in parentheses are in percentage

Table 5: Tomita scores and the likelihood of 6-month survival

Tomita <i>et al.</i> score groups	Median survival time months	95% CI months	Survival (months)	
			<6 months	>6 months
0-3	15	10-20	6 (21.4)	22 (78.6)
4-6	9	8-10	8 (27.6)	21 (72.4)
7-8	4	3-5	20 (58.8)	14 (14.2)
9-10	2	1-3	10 (90.9)	1 (9.1)

Figures in parentheses are in percentage

Table 6: Odds of 6-month survival according to Tomita score (with score group 9-10 as reference group)

Tomita <i>et al.</i> score group	Log rank test	Odds ratio	95% CI
Score 0-3	$P = .002$	36.7	3.9 to 346.2
Score 4-6	$P = .004$	26.2	2.9 to 239.5
Score 7-8	$P = .078$	7.0	0.8 to 61.1

With a Tokuhashi score of 7 or more and a Tomita score of 6 or less there is more than 50% chance that the patient will survive beyond 6 months after surgery. The assurance that there is a good chance of survival after surgery can be useful for surgeons as it will give them the confidence to proceed with surgery. This knowledge will also be useful when counseling patients on various treatment options.

Survival logistic analysis at 6 months: Tomita vs Tokuhashi score

Stepwise logistic regression analysis was used to evaluate the strength of correlation between the Tokuhashi and Tomita scores and 3-month and 6-month survival. The Tomita score ($P = .001$) was shown to be a significant independent predictor for 3-month as well as 6-month survival. The Tokuhashi score was not used as it was not a significant predictor in comparison with the Tomita score for 3- and 6-month survival.

We examined survival in the different score groups, with the Tomita 9-10 score group (i.e., poorest prognosis) as the reference group; the 6-month survival in the groups is shown in the Table 6.

DISCUSSION

In patients with metastatic spinal tumors surgery can provide symptomatic relief of pain and nerve palsy and improve quality of life.^{7,13-15} However, because of the morbidity

associated with surgery and the recuperation period required, patients considered for surgical intervention should have a reasonable life-expectancy (of at least 3-6 months) postoperatively.¹⁶

According to the revised Tokuhashi preoperative prognostic scoring system, total scores of 0-8, 9-11, and 12-15 predict life-expectancy of <6 months, >6 months, and ≥ 1 year, respectively. Tokuhashi *et al.* found that with this scoring system the survival period after surgery could be predicted consistently. The accuracy rate was 86.4% in a prospective series of 118 patients and 82.5% in a retrospective series of 246 patients.¹²

Tomita *et al.*¹³ used three factors for estimating survival prognosis: the grade of malignancy, extent of visceral metastases, and extent of bone metastases. Each factor was assigned a weighted score, which was determined retrospectively. Visceral metastases have twice the weightage as bony metastases, reflecting the relatively stronger correlation of the former with prognosis (which was apparent in our study also). Tomita *et al.* applied this scoring system prospectively to a series of 61 patients with spinal metastases between 1993 and 1996. In 43 of 52 patients (83%) who had been treated surgically they achieved local control for more than 80% of the survival period (the life span of the patient). The results suggested that this classification was simple to use, had prognostic value, and was reliably accurate in the management of spinal metastases.

The KPS has been used in oncology since 1948 to assess performance status of patients.¹⁹ It is generally regarded as the gold standard measurement of performance status in cancer patients.^{17,18} Our study showed that the KPS had the highest correlation with survival ($P = .000$, log rank test). Being a general score, it takes into account many comorbidities that determine survival. There is higher median survival time for the female population in our study [$P < .05$, log rank test]. Of females with breast cancer, 93% had KPS of more than 60%.

The efficacy and accuracy of the Tokuhashi and Tomita scoring systems has been studied by many authors in the past in different population groups. Grainger *et al.*²⁰

retrospectively reviewed 169 patients operated for spinal metastasis and calculated prognostic scores according to the systems of Tokuhashi and Tomita. They found that patients with Tokuhashi scores of 9–12 had 50% survival of 23 months compared to 5 months and 2 months survival in those with scores of 5–8 and 1–4, respectively ($P < .05$). The Tomita scoring method showed a similar trend, with 50% survival of 15 and 5 months for predicted long and medium term groups ($P < .05$). The authors concluded that both systems are potentially useful when deciding the suitability for surgery of patients with metastatic spinal disease. They had concluded that the Tomita system was less sensitive for early mortality.

Ulmar *et al.*²¹ retrospectively analyzed 37 patients surgically treated for vertebral metastases secondary to renal cancer. The Tokuhashi and Tomita scores were calculated for each patient. They found that the Tokuhashi score was very reliable for the estimation of life-expectancy of renal cancer patients with vertebral metastases, with a statistically high significance. However, they found no correlation between predicted and real survival with the Tomita score.

Zeng *et al.*,²² in their retrospective review, used the revised Tokuhashi system to score 447 patients operated for spinal metastases. The relationship between survival time and the Tokuhashi score was analyzed. They concluded that the Tokuhashi score was positively correlated with survival time ($r = 0.833$; $P < .001$). Thus, with a revised Tokuhashi score of 12–15 points, surgery would be a good option for extending lifespan in a patient with a solitary spinal metastasis of a slow-growth primary tumor.

Katagiri *et al.*²³ did a multivariate analysis of data from 350 patients operated for spinal metastases. They identified five significant prognostic factors for survival, namely, the site of the primary lesion, the performance status, the presence of visceral or cerebral metastases, any previous chemotherapy, and presence of multiple skeletal metastases. The score for each significant factor was derived from the corresponding estimated regression coefficients (natural logarithm of the hazard ratio). The prognostic score was calculated by adding up the scores for the individual factors. The rate of survival was 31% at 6 months and 11% at 1 year for patients with a prognostic score of 6 or more. By contrast, patients with a prognostic score of 2 or less had a rate of survival of 98% at 6 months and 89% at 1 year. This scoring system can be used to determine the optimal treatment for patients with pathological fractures or epidural compression.

Our study analyzed all six components of the Tokuhashi scoring system and found that the three parameters that significantly influence survival without controlling the other

variables were the individual performance score, extent of metastasis to visceral organs, and extent of extraspinal bone metastases.

The type of primary tumor was not found to be statistically significant in the revised Tokuhashi scoring system, which had five grades ($P = .9131$ log rank), but it was found to be significant with the original scoring system where the score was categorized to three grades ($P = .027$). This may be explained by the lack of power of the study when the categories were expanded from three possibilities to six in the revised score.

Similar to previous studies that have proved the efficacy of both the Tokuhashi and the Tomita scoring systems, we too found that both scores correlated well with survival. Stepwise logistic regression for 3 and 6 months survival revealed that the Tomita score correlated more closely with survival than the Tokuhashi score, which is in contrast to findings of the earlier studies. The Tokuhashi scoring system takes into account parameters that do not significantly influence survival (e.g., presence of spinal cord palsy and number of vertebral levels involved) and this may confound the final score. Satoshi *et al.* found that, in patients with lung cancer, among the components of the Tokuhashi score only the patient's performance status correlated with survival, and that the Tokuhashi score as a whole did not correlate with survival.²⁴

CONCLUSION

The individual performance status, extent of visceral metastasis, extent of bone metastases, and tumor activity are significant predictors of survival in patients with metastatic disease of the spine and requiring surgery. Both the revised Tokuhashi score and the Tomita score were significantly correlated with survival. A revised Tokuhashi score of 7 or more and a Tomita score of 6 or less indicated more than 50% chance of surviving 6 months postoperatively. We recommend that the Tomita score be used for prognostication in patients who are contemplating surgery as it is simpler to score and has a higher strength of correlation with survival than the Tokuhashi score.

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REFERENCES

1. Abrams HL, Spiro R, Goldstein N. Metastases in carcinoma: Analysis of 1000 autopsied cases. *Cancer* 1950;3:74-85.
2. Fornasier VL, Horne JG. Metastases to the vertebral column. *Cancer* 1975;36:590-4.

3. Gerszten PC, Welch WC. Current surgical management of metastatic spinal disease. *Oncology (Williston Park)* 2000;14:1013-24.
4. Hatrick NC, Lucas JD, Timothy AR, Smith MA. The surgical treatment of metastatic disease of the spine. *Radiother Oncol* 2000;56:335-9.
5. Klimo P Jr, Kestle JR, Schmidt MH. Clinical trials and evidence-based medicine for metastatic spine disease. *Neurosurg Clin N Am* 2004;15:549-64.
6. Maranzano E, Trippa F, Chirico L, Basagni ML, Rossi R. Management of metastatic spinal cord compression. *Tumori* 2003;89:469-71.
7. Tokuhashi Y, Kawano H, Ohsaka S, Matsuzaki H, Toriyama S. A scoring system for preoperative evaluation of the prognosis of metastatic spine tumor prognosis. *J Jpn Orthop Assoc* 1989;63:482-9.
8. Karnofsky DA. Clinical evaluation of anticancer drugs: Cancer chemotherapy. *GANN Monogr* 1967;2:223-31.
9. Citrin DL, Hougen C, Zweibeil W, Schlise S, Pruitt B, Ershler W. The use of serial bone scans in assessing response of bone metastases to systemic treatment. *Cancer* 1981;47:680-5.
10. Swenerton KD, Legha SS, Smith T, Hortobagyi GN, Gehan EA, Yap HY. Prognostic factors in metastatic breast cancer treated with combination chemotherapy. *Cancer Res* 1979;39:1552-62.
11. Yamashita K, Yonenobu S, Fuji T: Staging of metastatic spinal tumor. *Rinsho Seikei Geka* 1986;21:445-50.
12. Tokuhashi Y, Matsuzaki H, Oda H, Oshima M, Ryu J. A revised scoring system for preoperative evaluation of metastatic spine tumor prognosis. *Spine* 2005;30:2186-91.
13. Tomita K, Kawahara N, Kobayashi T, Yoshida A, Murakami H, Akamaru T. Surgical strategy for spinal metastases. *Spine* 2001;26:298-306.
14. Tokuhashi, Matsuzaki H, Oda H, Oshima M, Ryu J. A revised scoring system for preoperative evaluation of metastatic spine tumor prognosis. *Spine (Phila Pa 1976)* 2005;30:2186-91.
15. Enkaoua EA, Doursounian L, Chatellier G, Mabesoone F, Aimard T, Saillant G. Vertebral metastases: A critical appreciation of the preoperative prognostic Tokuhashi score in a series of 71 cases. *Spine* 1987;22:2293-8.
16. Walker MP, Yaszemski MJ, Kim CW, Talac R, Currier BL. Metastatic disease of the spine: Evaluation and treatment. *Clin Orthop Relat Res* 2003;415:S165-75.
17. Kaasa T, Wessel J. The Edmonton Functional Assessment Tool: Further development and validation for use in palliative care. *J Palliat Care* 2001;17:5-11.
18. Nikolett S, Porock D, Kristjanson LJ, Medigovich K, Pedler P, Smith M. Performance status assessment in home hospice patients using a modified form of the Karnofsky Performance Status scale. *J Palliat Med* 2000;3:301-11.
19. Karnofsky D, Abelmann W, Craver L, Burchenal J. The use of nitrogen mustard in the palliative treatment of cancer. *Cancer* 1948;1:634-56.
20. Grainger M, Stirling A, Marks D. validation of Tokuhashi and Tomita prognostic scoring systems in spinal metastases. *JBJS(Br)* 2004;86-B:SUPP_III, 293.
21. Ulmar B, Naumann U, Catalkaya S, Muche R, Cakir B, Schmidt R, *et al.* Prognosis scores of Tokuhashi and Tomita for patients with spinal metastases of renal cancer. *Ann Surg Oncol* 2007;14:998-1004.
22. Zeng JC, Song YM, Liu H, Gong Q, Li T, Liu LM, *et al.* The predictive value of the Tokuhashi revised scoring system for the survival time of patients with spinal metastases. *Sichuan Da Xue Xue Bao Yi Xue Ban* 2007;38:488-91.
23. Katagiri H, Takahashi M, Wakai K, Sugiura H, Kataoka T, Nakanishi K. Prognostic factors and a scoring system for patients with skeletal metastasis. *J Bone Joint Surg Br* 2005;87:698-703.
24. Ogihara S, Seichi A, Hozumi T, Oka H, Ieki R, Nakamura K, *et al.* Prognostic factors for patients with spinal metastases from lung cancer. *Spine* 2006;31:1585-90.

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