



New Predictive Index for Survival in Symptomatic Spinal Metastases

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■ **OBJECTIVE:** Patients with spinal metastases have broad variability in morbidity, mortality, and survival. Existing prognostic scoring systems have limited predictive value. Our aim is, given recent advances in surgical and medical care for patients with cancer and spinal metastases, to develop a new survival index with superior prognostic value.

■ **METHODS:** We completed a retrospective analysis on 77 patients who received surgery for metastatic tumors to the spine, of patient factors like pathologic subtype, age, neurologic examination, type of surgical procedure, Hauser Ambulation Index, and a novel scoring system for degree of tumor burden in several organ systems, among others. A survival index will be derived from the patient factors that, when measured preintervention, best predicted survival post intervention.

■ **RESULTS:** Although primary organ or pathologic type was not predictive of survival for patients with metastatic disease in this population, the degree of lung tumor burden (LTB) and preoperative Hauser Ambulation Index were predictive of survival. After a multivariable analysis of >20 different patient factors, the Jenkins Survival Index (JSI, a 0–21 scale) was constructed using a machine-learning system as the sum of the HAI (0–9 scale) and LTB score (0–3 scale) multiplied by 4 ($JSI = HAI + 4 \cdot LTB$, $Rho = -0.588$, $P < 0.0001$). The JSI had a positive predictive value of 92% compared with 54.1% and 56.9% for Tokuhashi and Tomita scales, respectively.

■ **CONCLUSIONS:** The JSI predicts in a meaningful way survival outcomes for patients symptomatic from spinal

metastases, which will be of value to oncologists and other clinicians treating patients with metastatic disease.

INTRODUCTION

Predicting the survival of patients with cancer is a challenge facing all clinicians who treat these patients.¹ Predicting long-term survival has been complicated by a number of factors, not the least of which is the evolving nature of medical treatments for various cancers.² Recently, more treatment options have been developed, making many cancers more manageable. Understanding the interrelationship of various factors and its impact on patient survival is critical to determining procedures, treatments, and other therapeutic options that are appropriate for a particular patient, given his or her likelihood of survival. It does not make sense to offer an extensive surgical procedure to patients who have at best a limited life expectancy, as they are unlikely to adequately recover from such a procedure before their life expectancy would run out.³ By the same token, if we could identify patients with significant longevity, then more extensive treatments that could potentially improve their quality and quantity of life should be undertaken as such patients could very well live long enough to reap the benefits from such procedures.

Spinal metastatic disease has a profound impact on a patient's quality of life, such as neurologic deterioration from spinal cord compression or pain from instability caused by fractures and deformities. Managing these conditions, especially in cancers not particularly amenable to noninvasive therapies such as radiation or chemotherapy, can be more challenging, when faced with the sequelae of a surgical treatment. Although there is a spectrum of surgical treatments available, ranging from minimally invasive to

Key words

- Neurosurgery
- Spine
- Survival index

Abbreviations and Acronyms

- **CCI:** Charlson Comorbidity Index
- **HAI:** Hauser Ambulation Index
- **JSI:** Jenkins Survival Index
- **KPS:** Karnofsky performance scale
- **MIS:** Minimally invasive surgery
- **ROC:** Receiver operating characteristic
- **TS:** Tumor stratification

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maximally invasive deformity correction procedures, all surgical procedures carry with them known consequences, as well as risks for complications. Known consequences include surgical pain, exposure to anesthesia, and a period of immobility and recovery. Potential complications are often related to the previously mentioned issues and include injury to neurologic elements not previously damaged; vascular and cerebrovascular or cardiovascular complications including deep venous thrombosis stroke and heart attacks; infections; and delayed spinal instability from nonunion or hardware failure.⁴ Any surgical treatment carries with it risks and benefits that need to be considered among all the alternatives.⁵ Understanding which patients have the greatest potential benefit from surgical operative treatments is critical to optimizing their care.

A number of individual factors have been put forth: oncologic diagnosis, mobility in neurologic function, degree of dissemination of tumor, presence of cerebral or spinal metastases, and others.⁶ Numerous spinal treatments and spinal predictive indices exist for patients with metastasis to the spine. In particular, the Tomita and Tokuhashi scales are widely used systems to predict survival and direct treatment options.⁶⁻⁸ In addition, there are a number of other functional indices and other predictive scales that have been attempted to be applied toward the management of patients with oncologic or neurologic disease including the Charlson Comorbidity Index, Hauser Ambulation Index (HAI, a mobility scale previously validated in the multiple sclerosis patient population), and Karnofsky performance scale (KPS).⁹⁻¹¹ Although it is generally understood that the healthier patients tend to live longer, quantifying which factors accurately predict survival, especially in patients whose cancer is advanced enough to have already spread to the spine, is a difficult and so far relatively unrewarding endeavor.¹²

There were a number of factors which we hypothesized might have an impact upon survival; in particular age of the patient at presentation, the degree of involvement of the various organ systems of the body (including lungs, liver, cardiovascular organs, brain, and spine), and oncologic diagnosis, in addition to the patient's ability to ambulate before the surgery, their ability to ambulate after the surgery, and their KPS score, among others. Although many authors have looked at the cell type of origin of cancer as a predictive factor, we have found that quantity of metastatic or primary lung disease seems to be more predictive of outcomes with patients of metastatic disease.^{13,14} It is our hypothesis that tumor types will distribute to the spine in similar numbers, across diagnoses and treatment strategies. And if these types do not predict survival, they should not be used to determine surgical spinal treatments.

Our hypothesis is that the amount of tumor burden, metastatic, primary, or both, within a particular organ system may be more predictive of survival than the cell type of origin of the tumor. We therefore also propose a new scoring system that is simple to apply and approximates the amount of tumor burden in each organ system. We call it the *tumor burden assessment*.

METHODS

All research performed was done under the supervision and approval of the Program for the Protection of Human Subjects at

Mount Sinai and adhered to all of their policies and procedures. Two pools of patients, a minimally invasive tumor group of 30 patients and a control group of 51 patients who had open tumor resection procedures, were pulled from the primary investigator's patient population and the Mount Sinai Data Warehouse. The open tumor resection group was used as a comparison group because it is considered the standard of care. This group was analyzed after being selected from a larger patient list by carefully screening for similar characteristics of the degree and quantity of tumor involved, the presence of epidural extension of the tumor (a requirement for surgical treatment), as well as the degree of dissemination and organ involvement of other organ systems. We expect similar distribution of tumors between the open and minimally invasive groups. We did not include all consecutively operated patients because the open surgery group had to be eligible for a minimally invasive approach to be matched with the minimally invasive surgery group. In addition, because this is a retrospective study, we were not able to include all surgeries prospectively and sequentially. All minimally invasive patients were included. All patients were surgically treated at a single institution (the Mount Sinai Hospital, New York, New York, USA).

All patients identified for inclusion had 1 or 2 spinal sites of disease with spinal cord compression, and no more than two vertebral bodies involved in tumor at that site. This was meant to identify patients for whom generally accepted practice would consider surgical candidates for 1 of several approaches, and to ensure a relatively homogenous population of tumor involvement in the spine for data analysis. All patients underwent some form of spinal surgery including minimally invasive and open procedures, decompressions, stabilization, fusions, or all of the above. In particular, before knowing what surgical procedure the patient underwent, the senior investigator (A.L.J.) evaluated all potential control patients and for each one determined that the patient would be a candidate for a minimally invasive surgical option. This was considered 1 of the inclusion criteria for the control group. As such, the senior investigator was blinded to treatment before selection for the control group.

In addition, patients who were managed nonsurgically were not included to keep cohorts as similar as possible and in order to eventually determine whether there was a survival difference between minimally invasive and open approaches. The open surgery group matched our minimally invasive group in terms of age, gender, tumor type, and baseline neurologic function. Also, these groups had no more than 2 levels of disease that were contiguous and no more than 2 noncontiguous areas (i.e., no more than 4 total areas involving vertebral body disease).

We may have other unintended biases including institutional, histologic, and age biases. Also, there is potential bias for those patients who elected not to undergo a surgical procedure and those who are unable to withstand anesthesia.

A chart review was performed to identify other patient characteristics that might impact the survival of patients with spinal metastases.

Physical Characteristics

Physical characteristics such as gender, age at time of treatment, height, and weight were calculated. A Hauser Ambulation Index was attempted to be calculated for all patients, but because the

open surgical group was from a diverse group of spinal surgeons, not all patients' preoperative neurologic examinations were adequately documented to determine the full Hauser Ambulation Index. Of these 81 patients, only 77 were able to be used for this assessment. Similarly, only the minimally invasive group had 100% adequate documentation from the preoperative examinations (either office or admission data) to determine a KPS score; ultimately we were able to calculate one for 30 patients. For the remaining 47 patients, however, after we determined that the HAI did correlate well with the KPS (Pearson $r = 0.75$, $P = 0.0000023$), we then estimated the KPS from the HAI by a multiplier of $-3.68 \cdot \text{HAI} + 82.09$. A scatter plot of the KPS score as a function of the Hauser Index with a regression line in the minimally invasive surgery (MIS) group is shown in **Figure 1**.

Because the nature of the condition frequently involved emergent surgery and emergent assessment, preoperative examinations were limited in some cases. As such, we attempted to reach out to a number of doctors but were not always able to get their data.

Charlson Comorbidity Index

The Charlson Comorbidity Index estimates 1-year mortality based on age, serum albumin, and comorbidities.¹⁵ For both MIS and open surgery groups, the Charlson comorbidity index (CCI) was calculated by assigning points weighted for the type of comorbidity. The relationship between CCI and survival was analyzed when selecting factors predictive of survival.

Tumor Aggressiveness Index

Tumor stratification was calculated on the basis of the American Cancer Society's data (Cancer Facts and Figures 2014) for overall tumor survival of the common cancer types. On the basis of their data, we identified the 5-year survival for each of the cancers in our group, and from those survival rates we came up with a relative stratification based on 5-year survival of each type of cancer, assuming that spinal metastases were considered distant metastatic disease.

Smith et al. (2016) reported on a patient sample from 2003–2009 that in 2014 the 5-year survival for various cancers was as follows: breast cancer (24%); colon cancer (13%); kidney cancer (12%); liver cancer and cholangiocarcinoma (3%); lung cancer (4%); oral cancer (36%); ovarian cancer (27%); prostate cancer (28%); myeloma (45%, with or without spinal metastases); and thyroid cancer (55%). Stratification 0, which was the shortest survival group, included hepatocellular carcinoma, cholangiocarcinoma (3%), and lung cancer (4%, all types). Stratification 1, which was the moderate survival group, included breast cancer (24%), myeloma (45%, but this does not include those with distant spread such as spinal metastases), colon cancer (13%), and melanoma (16%). Stratification 2, with the longest average survival, included ovarian cancer (27%), prostate cancer (28%), squamous (oral) carcinoma (36%), central nervous system lymphoma (69%, but not specific to spine), and liposarcoma (70%–80%, but not specific to spine).¹⁶

Tomita and Tokuhashi Scores

The Tomita and Tokuhashi scores are prognostic scoring systems that estimate survival for patients with spinal metastases.^{14,17} The Tomita score is the sum of a numeric value based on the type of

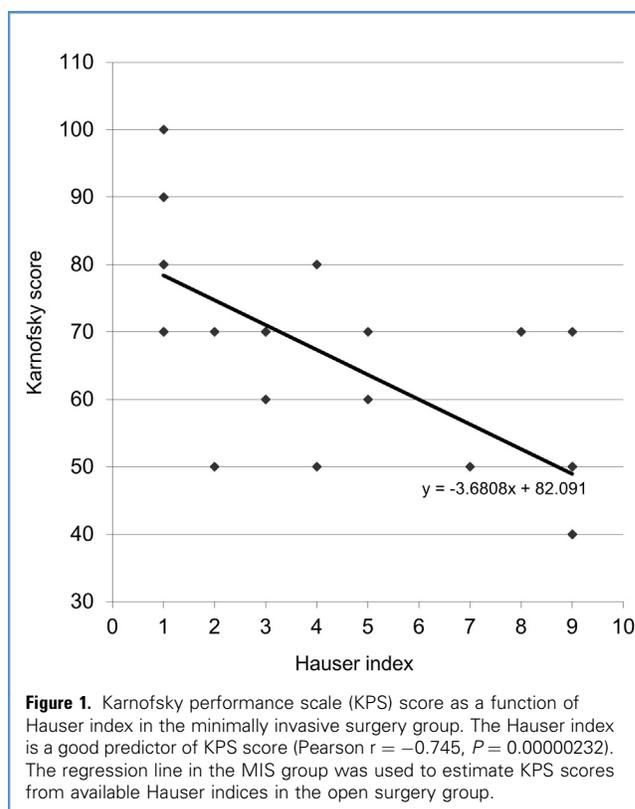


Figure 1. Karnofsky performance scale (KPS) score as a function of Hauser index in the minimally invasive surgery group. The Hauser index is a good predictor of KPS score (Pearson $r = -0.745$, $P = 0.00000232$). The regression line in the MIS group was used to estimate KPS scores from available Hauser indices in the open surgery group.

primary tumor; a numeric value based on the presence of visceral metastases and whether they are treatable (according to the surgeon performing the evaluation, a subjective assessment); and whether there are solitary or multiple bone metastasis. The Tokuhashi score considers patient KPS, number of extraspinal bone metastases, number of metastases in the vertebral body, metastases to major internal organs and whether they are removable, primary cancer site, and neurologic deficits. Tomita and Tokuhashi scores were calculated for all patients, although for the patients in whom a KPS score was not available, we used estimated KPS from the HAI (with a multiplier $-3.6808 \cdot \text{HAI} + 82.091$, see “Physical Characteristics” earlier). Tomita scores 2–4 and Tokuhashi scores 12–15 were defined as predictive of survival of more than 1 year.¹⁸

Tumor Burden Assessment

We presumed that the degree of involvement with certain key organ systems would result in progressive physical impairment and ultimately predict poor survival. The total amount of tumor within a particular organ or organ system was assessed for each patient, and to grade this involvement, we developed a new scoring system of the tumor burden within each organ system. This involvement was rated on a scale of 0–3 for the following systems: cardiovascular, kidney and adrenal, skull and brain, lung, liver/pancreas, and spine or spinal cord. A score of 0 was given if there was not metastasis in that specific organ system. A score of 1 was given if there was a single tumor metastasis in the organ system that was <2 cm in diameter. A score of 2 was given if there

was 1 small metastasis (<2 cm in diameter) with surrounding edema, if there were multiple smaller metastases (<2 cm), or if there was 1 larger metastasis (2–4 cm). A score of 3 was given if there was disseminated growth, 2 or more lesions with edema, or multiple involvements within the organ system.

Each organ system was scored according to the system described earlier. Organ system scores found to be significantly predictive of survival on an individual basis will be incorporated into the final index. Three raters (Wei, Nistal, and Martini) then rated the subjects using the Tokuhashi¹⁴ and Tomita¹⁷ scoring systems and our final index. The scores for all 3 indices will be compared on the basis of predictive value.

Data Analysis

Multiple regression analyses and univariate analyses were used to determine significance of relationship between the study variables and survival. Spearman's rho was used to investigate the relationship between scores and survival. All reported *P* values are set with standard $\alpha = 0.05$. Statistical analyses were performed using SAS (SAS Institute; Cary, NC).

A weighted model was derived from a generalized linear model.^{19,20} Receiver-operating characteristic (ROC) curves were used to assess relative predictive value of Tomita, Tokuhashi, and our index.²¹ The generalized linear model and ROC analyses were performed using the R language for statistical programming (R Foundation for Statistical Computing; Vienna, Austria).

RESULTS

Age

In the MIS group the average age was 62.03 and standard deviation (STD) was 11.80. In the open group the average age was 58.75 (STD = 12.45). Total average (across both groups) was 59.96 (STD = 12.24). Ages in the MIS and open groups were not significantly different (Student's *t*-test, *P* = 0.245, NS).

Tumor Type

In the MIS group there was a large variety of primary tumor types and locations: breast, colon, central nervous system, cholangiocarcinoma, hepatocellular carcinoma, non-small lung cancer, adenocarcinoma, melanoma, non-Hodgkin lymphoma, liposarcoma, ovarian, prostate, and oral squamous cell carcinoma. In the open group there was also a large variety of primary tumor types and locations: bladder, breast, colon, esophagus, lung, myeloma, non-Hodgkin lymphoma, pancreas, prostate, renal, thyroid, hepatocellular carcinoma, uterine, and tongue.

Treatment Data

Of 30 MIS patients, 24 of them (80%) received preoperative or postoperative radiation and 25 (83%) received chemotherapy. Of 51 open surgery patients, 38 of them (74%) received preoperative or postoperative radiation and 38 of them (74%) received chemotherapy.

There was no statistically significant difference (*P* = 0.60, Fisher exact test) in the rates of patients who received radiation in the MIS and open surgery groups (80% vs. 74%). There was also no significant difference (*P* = 0.52, Fisher exact test) in the rates of

patients who received chemotherapy in the MIS and open surgery groups (83% vs. 74%).

Tumor Stratification

Tumor stratification (TS) scores were 0, 1, and 2. Average TS in the MIS group was 0.83, and in the open group it was 1.02. The total average was 0.95. There was no significant difference between tumor stratification in the MIS and open groups (chi square test, *P* = 0.552, NS).

Charlson Comorbidity Index

In the MIS group the average CCI was 7.53 (STD = 2.11), and in the open group the average CCI was 7.33 (STD = 2.19). The total average was 7.41 (STD = 2.15). CCI in the MIS and open groups was not significantly different (Student's *t* test, *P* = 0.689, NS).

Karnofsky Performance Scale Score

In the MIS group the average KPS score was 67 (STD = 12.1), and in the open group the average KPS score was 66.9 (STD = 11.8). Total average was 66.9 (STD = 11.8). KPS scores in the MIS and open groups were not significantly different (Student's *t*-test, *P* = 0.971, NS). Noteworthy is that in the open group, the KPS score was estimated from HAI (0 of HAI predicted 82.1 of KPS, 1–78.4, 2–74.7, 3–71.0, 4–67.4, 5–63.7, 6–60.0, 7–56.3, 8–52.6, 9–49.0).

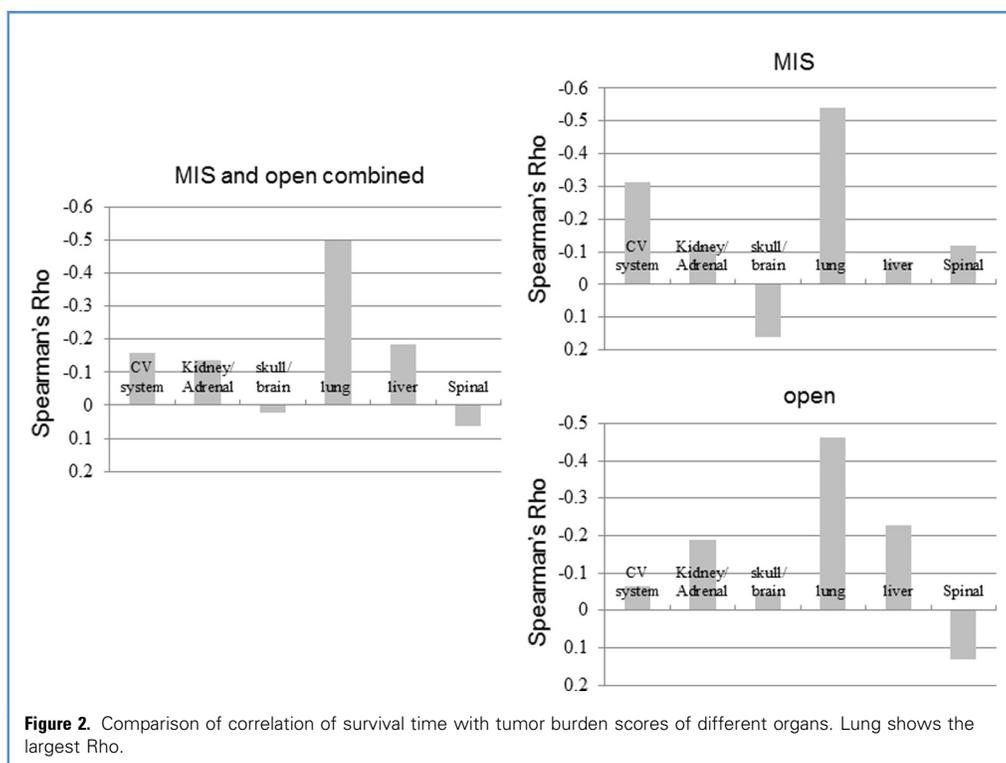
Hauser Ambulation Index

In the MIS group the average HAI before operation was 4.10 (STD = 3.28), and in the open group the average HAI was 4.13 (STD = 3.21). Total average was 4.12 (STD = 3.22). HAI in the MIS and open groups was not significantly different (Student's *t*-test, *P* = 0.971, NS).

Combined Analysis

In 4 patients with open surgery we were unable to identify or retrospectively recreate a Hauser ambulation score for them at the time of admission or immediately before surgery, and therefore results of these patients were not included in our analysis. Of the remaining 77 patients, Spearman Rho between tumor burden scores of different organs (CV system, kidney/adrenal, skull/brain, lung, liver, spine, total score of all systems) and survival times were calculated. Rho values are presented in **Figure 2**. In addition, Spearman Rho was calculated between survival time and multiple different patient characteristics that could be identified before a surgical procedure including Hauser ambulation index (HAI) and age of patient.

The survival time was the most strongly correlated with 2 variables—presence of lung cancer and patient ambulation just before surgery. The largest absolute value of correlation coefficient with survival time was found for lung cancer (Rho = -0.425) followed by Hauser ambulation index (Rho = 0.357). Correlations of age and cancer in other organs with patient's survival time were substantially smaller. Regression analysis based on the Cox proportional hazards model showed again the largest effect of lung (*P* < 0.0001) followed by HAI (*P* = 0.0025) with much smaller effects of other systems (spinal [*P* = 0.0378], liver [*P* = 0.2010]). Tumors of other organs (CV, kidney, brain) and other studied variables did not reach a minimal threshold level of *P* < 0.25 to be entered in



the stepwise selection process. The summary of stepwise selection of effects for this analysis is shown in **Table 1**.

On the basis of these findings, we propose a new burden index (Jenkins Survival Index [JSI]), which consists of a weighted sum of these 2 scores: presence of lung cancer and ambulation level before operation (note that smaller ambulation scores in HAI indicate better ambulation level).

To optimize the survival predictive time of JSI, we adjusted the weights of 2 subscores: “lung tumor burden score” and “HAI before surgery.” Lung tumor burden has a range of 4 units (scores

between 0 and 3), and presurgery HAI has a range of 10 (scores between 0 and 9). Using a generalized linear model, our calculation showed that optimal JSI index should be equal to $4 \cdot \text{Lung score} + 1 \cdot \text{HAI}$ to achieve the strongest correlation with survival time. JSI with such weights of lung and ambulation subscores showed substantially improved correlation with patient survival time ($Rho = 0.58, P < 0.00001$) as compared with a simplified JSI with equal weight of lung and ambulation subscores ($Rho = 0.49, P = 0.00001$).

Survival times of individual patients as a function of JSI scores (with $4 \times$ larger weights assigned to lung than pre-HAI scores) are presented in **Figure 3**. Distribution of data points in the plot (with linear regression $y = -0.1229x + 2.5369$) shows that JSI is a good predictor of survival time. Stronger presence of lung cancer accompanied by poorer ambulation before surgery predicts a shorter survival time of patients.

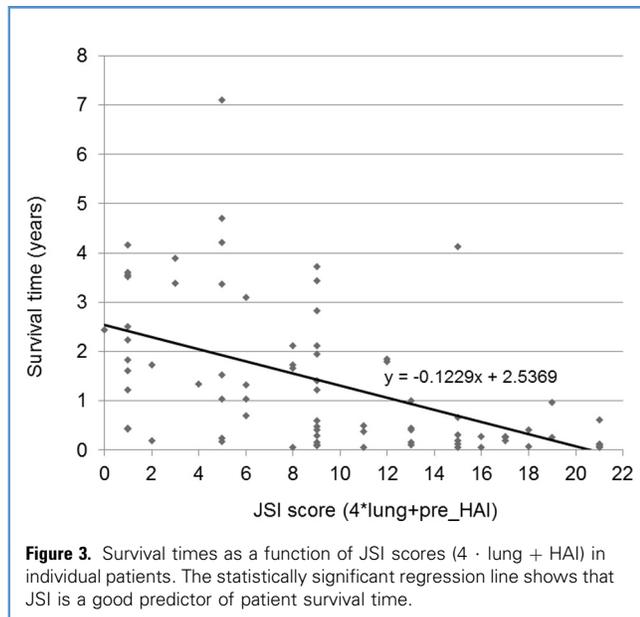
Table 1. Regression Analysis of Survival Data Based on Cox Proportional Hazards Model: Lung Followed by HAI Shows Largest Significance in Stepwise Selection

| Step | Entered | Removed | DF | Score Chi-Square | Wald Chi-Square | Pr >ChiSq |
|------|-----------|---------|----|------------------|-----------------|-----------|
| 1 | Lung | | 3 | 27.3158 | | <0.0001 |
| 2 | HAI | | 1 | 9.1643 | | 0.0025 |
| 3 | Group | | 1 | 3.0949 | | 0.0785 |
| 4 | Spinal | | 3 | 8.4303 | | 0.0379 |
| 5 | Tum_strat | | 2 | 5.4764 | | 0.0647 |
| 6 | CCI | | 1 | 3.7008 | | 0.0544 |
| 7 | Liver | | 3 | 4.6302 | | 0.2010 |
| 8 | | Liver | 3 | | 4.4238 | 0.2192 |

Comparison with Tokuhashi and Tomita

We compared correlation with survival time of JSI with other existing tumor burden indexes in the literature including Tokuhashi, Tomita, and other tumor burden indexes: comorbidity index and tumor stratification index (based on historical data of survival time of patients with particular primary tumors).

Comparisons of correlation with survival time of JSI and other existing literature tumor burden scores are shown in **Figure 4**. The largest absolute value of correlation with survival had a JSI score ($Rho = 0.588, P < 0.00001$), followed by a Tokuhashi score ($Rho = 0.533, P < 0.00001$). Tomita was not significantly correlated with survival time ($Rho = 0.070, P = 0.55, NS$). The



Hauser ambulation index before operation (HAI), when used as a single measure predictor of survival, was significantly correlated with survival ($Rho = 0.357, P = 0.00145$) and was a much better predictor of survival than Tomita.

In an ROC curve analysis, the weighted JSI had a more superior area under the curve than the Tokuhashi and Tomita scores, demonstrating that the JSI has greater predictive value for 1-year mortality (Figure 5). Area under the curve was 0.76 for JSI, 0.54 for Tokuhashi, and 0.57 for Tomita. The specificity of the JSI was 94.6% compared with 8.1% and 32.4% for Tokuhashi and

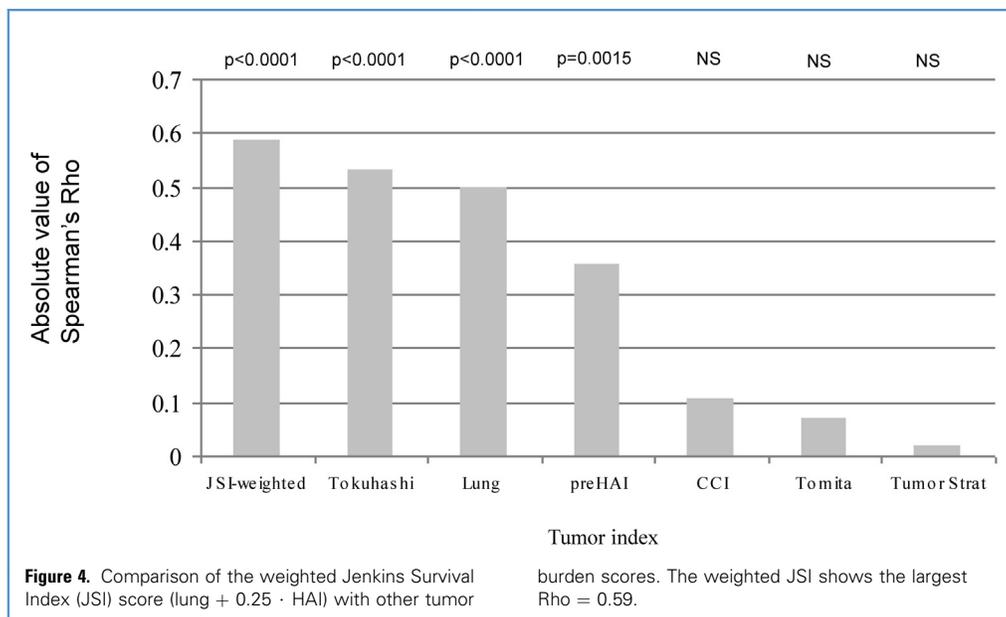
Tomita, respectively. The positive predictive value for the JSI was 92.0% compared with Tokuhashi and Tomita at 54.1% and 56.9% (Table 2).

DISCUSSION

The JSI offers a practical clinical tool for predicting survival in patients with metastatic tumors to the spine. Previous studies such as Fehling et al,²² Lei et al,²³ and Pereria et al¹³ have tried to address this issue of predicting survival in patients with metastatic tumors to the spine in recent years. However, compared with previous predictive indices, the JSI is able to make a prognosis with greater specificity and positive predictive value. This gives the JSI particular clinical value in identifying patients with 1-year mortality. The high accuracy of the JSI in identifying 1-year mortality, in contrast to the Tokuhashi and Tomita scores, would help clinicians identify patients who are least likely to improve with an open, or extensive, surgery.

For our patient population, there was an adequate distribution of tumors across different sites in each group, with no obvious difference in distribution between the 2 groups. We found that in this population of patients who have spinal metastatic disease and who require surgical intervention because of neurologic deterioration, they stratify well despite primary tumor diagnosis or presence of significant metastatic disease in other organs. Therefore these factors should not be considered in surgical treatment strategy.

Our analyses show that tumor burden in the lung is by far the most important consideration in patient prognosis compared with other organ systems. Furthermore, the Hauser ambulation index used in the JSI is independently a significant predictor of survival and measure of baseline health. Lung score and Hauser were both highly predictive with 4:3 relative weights on prognosis. Liver



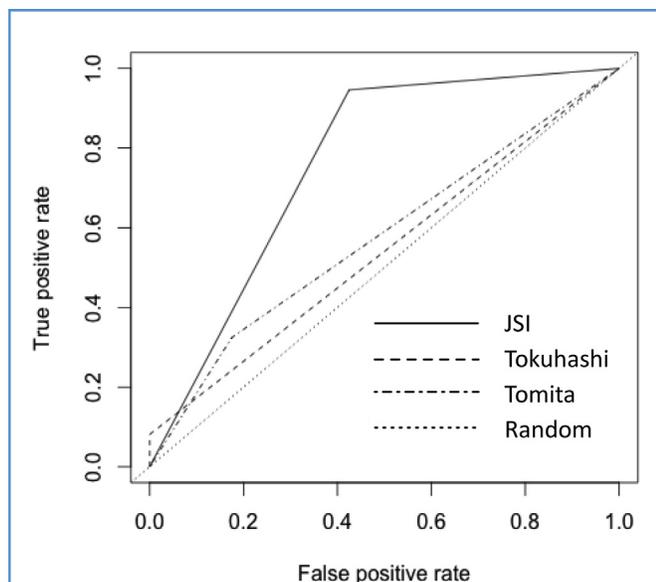


Figure 5. A receiver operating characteristic showing a true positive rate as a function of the false-positive rate.

tumor burden score was initially found to be significantly related to survival, but a generalized linear model found it to have insignificant predictive value relative to lung score and Hauser.

In creating a weighted version of the JSI, we chose to maximize specificity at the expense of sensitivity in identifying patients with 1-year mortality. A high sensitivity clinically translates to having only patients who will not benefit from surgery getting excluded from surgery. The accuracy of the JSI in identifying patients who should not receive surgery would enhance surgical outcomes and quality of life for patients through minimizing incorrectly excluding patients from intervention. Sensitivity for 1-year mortality would have lower utility in surgery for spinal metastasis. Patient outcomes for spinal metastases have been historically difficult to predict and are highly variable. By helping to exclude only patients with the worst prognoses, the JSI provides prognostic information with high accuracy and gives surgeons more capacity to tailor their treatments for the particular circumstances of each patient.

Table 2. Sensitivity, Specificity, and Predictive Values of Prognostic Scores

| | Weighted Jenkins Survival Index | Tokuhashi | Tomita |
|---------------------------|---------------------------------|-----------|--------|
| Sensitivity | 57.5% | 100.0% | 82.5% |
| Specificity | 94.6% | 8.1% | 32.4% |
| Positive predictive value | 92.0% | 54.1% | 56.9% |
| Negative predictive value | 67.3% | 100.0% | 63.2% |

In contrast, the Tokuhashi and Tomita scales are weighted toward sensitivity in identifying patients with 1-year mortality. The positive predictive values of these scales are close to chance, with 54.1% for Tokuhashi and 56.9% for Tomita. These predictive scales err on the side of excluding more patients from treatment, which discourages clinicians from treating patients who would benefit from intervention. The Tokuhashi and Tomita scales are further limited by their complexity, with each scale involving radiologic examination and categorization of tumor burden for multiple organ systems. The JSI is comparatively easier to assess and considers only tumor burden in the lung and ambulation. The ease of calculating the JSI further enhances its clinical utility for clinicians.

The JSI, although an index that is simpler to calculate and considers fewer variables than the Tokuhashi and Tomita, has significantly superior predictive ability ($P < 0.0001$). This was maintained across multiple modalities of analysis including quantitative association with length of survival post surgery and the categorical prognosis of 1-year mortality. The high sensitivity and low specificity of the Tokuhashi and Tomita demonstrate that they less accurately predict mortality for most patients in our current series. Previous literature, including recently published studies, has validated these predictive indices using patient data that are often more than a decade old.^{18,24,25} The Tokuhashi and Tomita do not reflect the advances made in oncology and spine surgery, and they have outlasted their clinical utility.

The utility of the JSI may extend beyond the spinal metastasis patient population. A regression analysis to identify organ systems associated with survival found that tumor burden in the spine was not significantly correlated with mortality. Although the JSI was developed from a population with spinal metastases, the fact that spinal metastases themselves were not significant predictors and do not factor into calculating the JSI suggests that the JSI may have applications in other oncologic patient populations. Furthermore, the components of the JSI suggest that severity of spinal metastases should not be used to disqualify patients from surgery.

A limitation of this study is that the number of patients included in analyses precluded dividing subjects into training sets and validation sets. The JSI was calculated from 1 patient population. The Tokuhashi and Tomita scales were developed through the same process. Future studies will involve application and assessment of the JSI on another patient population for external validity. This is a preliminary report of a new index. We plan on validating a grading system of organ involvement, as well as applying this grading system to a broader spectrum of patients other than those requiring surgical intervention eligible for a minimally invasive approach to see if predictive index has benefit for optimizing treatment for patients with spinal metastatic disease.

CONCLUSION

The JSI is a simple predictive index with superior performance to Tokuhashi and Tomita in determining prognosis for patients with spinal metastases who will undergo surgical intervention. This patient population has historically had highly variable survival rates, and the development of an accurate prognostic scale would

help improve quality of life for many patients. The prognoses estimated with JSI have high accuracy and may have substantial value for clinicians in determining which patients with spinal metastases would most benefit from surgery.

We feel that the low P values speak to the accuracy of the index and delaying publication for access to a larger data set would delay access for clinicians who could use the index to determine treatments while we resolve the training sets.

REFERENCES

- Ulmar B, Naumann U, Catalkaya S, et al. Prognosis scores of Tokuhashi and Tomita for patients with spinal metastases of renal cancer. *Ann Surg Oncol*. 2007;14:998-1004.
- Ulmar B, Reichel H, Catalkaya S, et al. Evaluation and modification of the Tomita score in 217 patients with vertebral metastases. *Onkologie*. 2007;30:414-418.
- Putz C, Wiedenhofer B, Gerner HJ, Furstenberg CH. Tokuhashi prognosis score: an important tool in prediction of the neurological outcome in metastatic spinal cord compression: a retrospective clinical study. *Spine (Phila Pa 1976)*. 2008;33:2669-2674.
- Kim J, Lee SH, Park SJ, et al. Analysis of the predictive role and new proposal for surgical strategies based on the modified Tomita and Tokuhashi scoring systems for spinal metastasis. *World J Surg Oncol*. 2014;12:245.
- Bhatt AD, Schuler JC, Boakye M, Woo SY. Current and emerging concepts in non-invasive and minimally invasive management of spine metastasis. *Cancer Treat Rev*. 2013;39:142-152.
- Laufer I, Rubin DG, Lis E, et al. The NOMS framework: approach to the treatment of spinal metastatic tumors. *Oncologist*. 2013;18:744-751.
- 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 (Phila Pa 1976)*. 1997;22:2293-2298.
- Mazenko GF. Spinodal decomposition and the Tomita sum rule. *Phys Rev E Stat Phys Plasmas Fluids Relat Interdiscip Topics*. 2000;62:5967-5977.
- Singh B, Bhaya M, Stern J, et al. Validation of the Charlson comorbidity index in patients with head and neck cancer: a multi-institutional study. *Laryngoscope*. 1997;107:1469-1475.
- Katagiri H, Takahashi M, Inagaki J, et al. Clinical results of nonsurgical treatment for spinal metastases. *Int J Radiat Oncol*. 1998;42:1127-1132.
- Ulmar B, Richter M, Cakir B, Muche R, Puhl W, Huch K. The Tokuhashi score: significant predictive value for the life expectancy of patients with breast cancer with spinal metastases. *Spine (Phila Pa 1976)*. 2005;30:2222-2226.
- Chen H, Xiao J, Yang X, Zhang F, Yuan W. Preoperative scoring systems and prognostic factors for patients with spinal metastases from hepatocellular carcinoma. *Spine (Phila Pa 1976)*. 2010;35:E1339-E1346.
- Pereira NRP, Janssen SJ, van Dijk E, et al. Development of a prognostic survival algorithm for patients with metastatic spinal disease. *J Bone Joint Surg Am*. 2016;98:1767-1776.
- Tokuhashi Y, Matsuzaki H, Toriyama S, Kawano H, Ohsaka S. Scoring system for the preoperative evaluation of metastatic spine tumor prognosis. *Spine (Phila Pa 1976)*. 1990;15:1110-1113.
- Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. *J Clin Epidemiol*. 1994;47:1245-1251.
- Smith HG, Memos N, Thomas JM, Smith MJF, Strauss DC, Hayes AJ. Patterns of disease relapse in primary extremity soft-tissue sarcoma. *Br J Surg*. 2016;103:1487-1496.
- Tomita K, Kawahara N, Kobayashi T, Yoshida A, Murakami H, Akamaru T. Surgical strategy for spinal metastases. *Spine*. 2001;26:298-306.
- Aoude A, Amiot LP. A comparison of the modified Tokuhashi and Tomita scores in determining prognosis for patients afflicted with spinal metastasis. *Can J Surg*. 2014;57:188-193.
- Tokuhashi Y, Uei H, Oshima M, Ajiro Y. Scoring system for prediction of metastatic spine tumor prognosis. *World J Orthoped*. 2014;5:262-271.
- Zheng B, Agresti A. Summarizing the predictive power of a generalized linear model. *Stat Med*. 2000;19:1771-1781.
- Zou KH, O'Malley AJ, Mauri L. Receiver-operating characteristic analysis for evaluating diagnostic tests and predictive models. *Circulation*. 2007;115:654-657.
- Fehlings MG, Nater A, Tetreault L, et al. Predictive factors for survival in surgical series of symptomatic metastatic epidural spinal cord compression: a prospective North American multicenter study in 142 patients. *Spine*. 2016;16:317-318.
- Lei M, Li J, Liu Y, et al. Who are the best candidates for decompressive surgery and spine stabilization in patients with metastatic spinal cord compression? A new scoring system. *Spine*. 2016;41:1469-1476.
- Eap C, Tardieux E, Goasgen O, et al. Tokuhashi score and other prognostic factors in 260 patients with surgery for vertebral metastases. *Orthop Traumatol Surg Res*. 2015;101:483-488.
- Anderson DC. ACP Journal Club. Review: statins do not increase risk for intracerebral hemorrhage. *Ann Intern Med*. 2012;156:JC3-JC6.

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