A VALIDATION OF THE OSWESTRY SPINAL RISK INDEX

Abstract

The purpose of this study was to validate the Oswestry Spinal Risk Index (OSRI) in an external population. The OSRI predicts survival in patients with metastatic spinal cord compression (MSCC).

We analysed the data of 100 patients undergoing surgical intervention for MSCC at a tertiary spinal unit and recorded the primary tumour pathology and Karnofsky Performance Status to calculate the OSRI. Logistic regression models and survival plots were applied to the data in accordance with the original paper. Lower OSRI scores predicted longer survival. The OSRI score predicted survival accurately in 74% of cases (p= 0.004).

Our study has found that the OSRI is a significant predictor of survival at levels similar to those of the original authors and is a useful and simple tool in aiding complex decision making in patients presenting with MSCC.

Keywords: spine; metastases; spinal cord compression; survival; prognosis.

Introduction

Metastatic cancer is one of the leading causes of death [1]. The skeletal system is the third most common site for metastases, and the spine is the most commonly affected part [1,2]. Ten year relative survival from cancer has increased from approximately 25% in the 1970s to 45% in 2007 across a range of cancers [3]. With significant improvements in survival for tumours with a predilection for spinal metastases (breast, prostate and renal cancer), the incidence of spinal metastasis is likely to increase. Approximately 20% of spinal metastasis cases exhibit neurological deficit due to spinal cord compression [4]. Untreated spinal metastasis results in the deterioration of life quality due to severe neurological deficits and intractable pain, which can shorten life expectancy with complications [5].

The primary aims of surgery in the treatment of metastatic spinal cord compression are to preserve or recover neurological function, treat spinal instability and provide pain relief with the aim of maintaining functional independence and quality of life [6]. Advances in adjuvant treatments necessitate a multidisciplinary approach that optimizes the combination of surgery, radiation therapy and chemotherapy to maximise tumour control and minimise the morbidity of treatment. Although the role of surgery remains largely palliative, appropriate adjuvant therapy may provide excellent localized tumour control [7].

The appropriateness of surgery and the proposed intervention are selected on the basis of predicted prognosis. Scoring systems are used to try to predict survival that will in turn guide treatment decisions. A wide range of scoring systems have been introduced in recent years with the intention of predicting survival and therefore guiding treatment in patients with spinal metastases e.g. Tomita [8], Tokuhashi [9] and Bauer [10]. Prognosis is affected by the patient's general condition [8], the primary tumour type [8], the presence of extra spinal bony metastases [9], the number of metastases in the vertebral body [9], the severity of spinal cord palsy [9] and the presence of any major organ metastases [8-10].

The scoring systems differ greatly in the kind of parameters assessed and the weights assigned to these parameters in the determination of the total score [8-10]. As a result, for the same patient, it is possible that different survival periods might be calculated and contradictory treatment strategies advised [11]. The National Institute for Clinical Excellence (NICE) has produced guidelines for the treatment of patients with MSCC. These guidelines have been produced to aid overall patient management- from educating the patient on which symptoms to be concerned about through to recommendations for cancer network services [12]. The guidelines suggest that surgery should be carefully planned to maximise the probability of preserving spinal cord function without undue risk to the patient, taking into account their overall fitness and prognosis. [13] Whilst an accurate prognosis is desirable there is often time pressure for treatment to be undertaken which limits the time available for repeat staging investigations. The best neurological outcomes following surgery for MSCC are achieved if surgery is carried out within 48 hours [13].
The urgency for intervention twinned with the need for an accurate prognostication method has driven the development of scoring systems.

The ideal scoring system can be applied to all patients, and be able to accurately and reproducibly predict survival in order to guide management. In recent years the revised Tokuhashi [9] and Tomita [8] scores have been widely used but validation studies have reported conflicting evidence in their ability to accurately predict survival [11,14]. Reliability may be increased in a sub-set of patients treated surgically [10, 15].

The Oswestry Spinal Risk Index (OSRI) is a scoring system developed by Balain *et al* [16] that predicts survival in patients with MSCC. It is derived from the most predictive variables of the revised Tokuhashi [9], Tomita [8] and modified Bauer [10]

scores. In a cohort of 199 patients with metastases, Balain *et al* [16] found the most important factors in predicting survival were the primary tumour pathology (PTP) and general condition (GC) of the patient based upon the Karnofsky score [17]. The PTP and GC are allocated scores and the formula: PTP + 2-GC is used to calculate the OSRI score. The lower the OSRI score, the longer the predicted survival of the patient.
The aim of this study was to carry out a validation of the OSRI.

Methods

Patients undergoing surgery for spinal metastases between January 2009 and November 2011 were identified from a prospectively recorded database at a tertiary referral centre for spinal surgery. The database records a detailed presenting history, past medical history, examination findings, investigation results and demographics. Electronic patient files were reviewed to identify those patients who had surgery for spinal metastases. Primary bone tumours of the spine and spinal cord tumours were excluded.

Patients were analysed considering their survival status as at July 2013. The analysis was undertaken retrospectively. The primary tumour and general condition score was recorded for each patient, as well as the date of birth, date of surgery and date of death if applicable. The PTP score was allocated based on this speed of growth of the primary tumour, as used in the Tomita scoring system [8]. The OSRI was then calculated for each patient. The assessor was not blinded as to whether the patient was dead or alive at the time of analysis.
A number of procedures were conducted to assess the validity of the OSRI score and its transferability across data sets; some of which are based on analyses presented by Balain *et al* [16]. Consistently with the analyses of Balain *et al* [16], and because of low numbers of patients in certain classes in the current analysis, patients classified with OSRI scores of 2 and 3, and patients classified with OSRI scores of 4 and 5 were combined into single classes. For all patients a Kaplan-Meier survival analysis was conducted to compare the survival experience of patients with varying OSRI scores. Median survival times and associated 95% confidence intervals were obtained for patients with each of the possible OSRI scores. Using the Mantel-Cox log rank statistic, pairwise comparisons of survival between patients in different groups were assessed.

Nagelkerke's pseudo-R^2 statistic was evaluated for a logistic regression analysis of patient survival using the OSRI score as a predictor and with patient age included in the model as a controlling variable. In this analysis the OSRI score was assumed to approximate to an interval-level variable, with mid-point coding given to combined groups. The Receiver Operating Characteristic (ROC) curve was also derived for the OSRI score and the area under the ROC curve calculated for the OSRI score variable to assess the capability of this index to distinguish between patients who survived to the end of the analysis period and those who died. An OSRI score corresponding to an optimal combination of sensitivity and specificity was also obtained.

Linearity of the model was checked by creating categorical variables corresponding to all values of the OSRI score, and assessing the linear trend of parameter coefficients. Cross-validation of the existing data set was facilitated by partitioning the data set into a training data set of 80% of the original cohort; and a validation set of the remainder. A logistic regression analysis was conducted on the training data set. Regression parameters obtained from this analysis were applied to the validation set and the level of predictive capability assessed on the validation data set.

Statistical significance in all inferential procedures was assumed to be indicated by p-values of <0.05.

Results

Analysis was undertaken on one hundred patients undergoing spinal surgery for spinal metastases between January 2009 and November 2011, aged between 19 and 88, with a mean age of 60.3 years (SD 12.4). The most common tumour type was breast (n=24) followed by lung (n=20). Seventy four patients died during the period of analysis; 26 survived until the end of analysis period and were hence recorded as censored observations.

Median survival times and associated confidence intervals for the entire cohort and for the patient groups according to their OSRI score are summarized in Table 1.

Table 1: Median survival times and confidence intervals for patients with differing OSRI scores

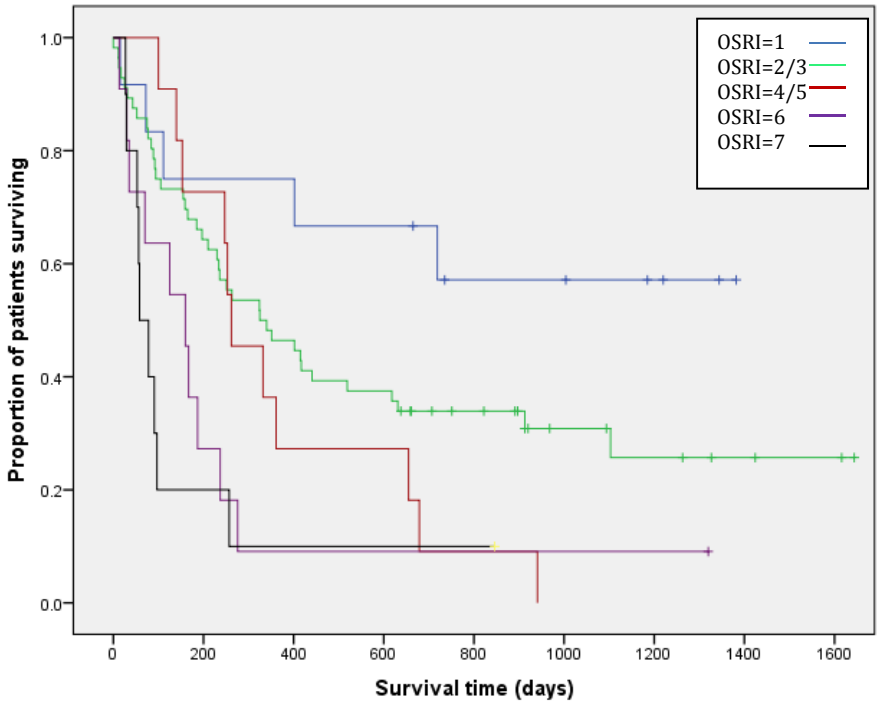
OSRI score	***Median survival time (days)***	***95% CI for survival time (days)***
1 (n=12)	*****	*****

2/3 (n=56)	***325***	***(140, 510)***
4/5 (n=11)	***262***	***(170, 354)***
6 (n=11)	***160***	***(55, 265)***
7(n=10)	***58***	***(24, 92)***
All patients (n=100)	***253***	***(165, 341)***

****Over 50% of patients survived in this group until the end of the analysis period***

Survival plots for each of the five OSRI classifications (Figure 1) shows distinct differences in survival experience, with greater survival being associated with lower OSRI scores.

Figure 1: Survival curves for patients with varying OSRI scores



Pairwise comparisons of survival between patients with OSRI score categories using the Mantel-Cox log rank statistic revealed substantive differences in survival experience between patients with OSRI scores 1 and 2/3. However survival experience between patients with other adjacent OSRI scores was not significantly different. Significant differences in survival experience between patients exhibiting greater modified OSRI score dissimilarity was observed; for example between patients with modified OSRI score 1 and patients with modified OSRI score of 4/5 or more; between patients with modified OSRI score 2/3 and patients with modified OSRI score of 6 or more; between patients with modified OSRI score 4/5 and

patients with modified OSRI score of 7. All log-rank statistics and associated p-values are summarized in Table 2.

Table 2: Mantel-Cox log-rank statistics and p-values for comparison of survival experience of patients with differing OSRI scores

OSRI score				
	2/3	4/5	6	7
1	2.82 (0.093)	7.07 (0.008)	7.12 (0.008)	8.07 (0.004)
2/3	-	1.47 (0.225)	5.37 (0.020)	8.43 (0.004)
4/5		-	1.67 (0.196)	4.17 (0.041)
6			-	0.477 (0.490)

Nagelkerke's pseudo-R^2 statistic of 0.145 was obtained for a logistic regression analysis of patient survival using the OSRI score as a single predictor, rising to 0.167 when patient ages were included as a controlling variable. The paper by Balain *et al* [16] proposing the OSRI found this score to have a Nagelkerke's pseudo R^2 statistic of 0.28. The hazard ratio of 1.75 obtained for the OSRI score in both models indicates that the hazard of death is raised by 75% for each advance in the OSRI score.

Model parameters from the logistic regression models are summarised in Table 3. It may be seen that while the OSRI score is a significant predictor of survival in both models, age is not a significant predictor in the controlled model. Examination of parameter coefficients in a model including all categories of the OSRI score as separate covariates verified the assumption of an approximate linear relationship between the OSRI score and the transformed outcome.

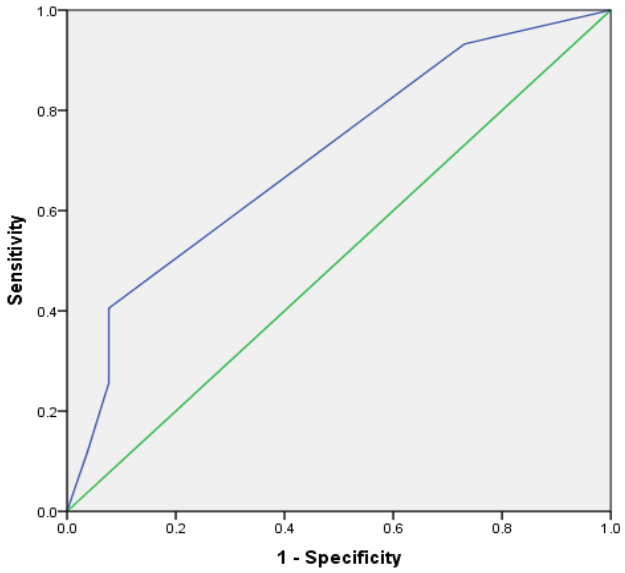
Table 3: Logistic regression model parameters

	Hazard ratio	***95% CI for hazard ratio***	***p-value***
Univariate model (Nagelkerke's R^2=0.167)			

OSRI score	***1.75***	***(1.19, 2.58)***	***0.004***
Controlled model (Nagelkerke's R^2=0.168)			
OSRI score	***1.75***	***(1.19, 2.57)***	***0.005***
Age	***1.01***	***(0.97, 1.05)***	***0.766***

Under the univariate model, 74 out of 100 patients (74%) were correctly classified: under the controlled model, 76 out of 100 patients were correctly classified (76%). The OSRI score was found to discriminate fairly well between patients who had died and those who had survived, with the area under the curve calculated to be 0.707. The ROC curve is illustrated in Figure 2.

Figure 2: ROC curve for OSRI scores, showing diagonal reference line (area under reference line =0.500)



Regression parameters derived from a logistic regression analysis of the training set applied to the validation set resulted in 14 out of 20 (70%) of cases being correctly predicted, a slight reduction from the value of 76% correctly predicted by applying the model to the full data set. The inclusion of age in the model did not affect predictive capability.

Discussion

In our analysis of patients who had undergone surgery for spinal metastases we found that the OSRI was a substantive predictor of survival; showing similar levels of performance to those obtained by Balain *et al* [16]. The value under the ROC curve of the OSRI score of 0.707 represents fairly good ability of this measure to discriminate between patients who survive and those who do not, and also corresponds closely to the concordance value of 0.67 for the OSRI index obtained by Balain *et al* [16]. A distinct deterioration in survival experience with increasing OSRI score is exhibited, as also found by Balain *et al* [16].

Significant differences in survival experience may generally be observed between patients with adjacent OSRI scores two or more categories apart. However, survival experience between patients with adjacent OSRI scores is less clear. This contrasts with the findings of Balain *et al* [16], who noted significant differences in survival between most patient sub-groups; upon which the OSRI score was originally based. Non-significant differences in survival times between patients exhibiting OSRI score dissimilarity may well be due to the fact that our study was limited to 100 patients, with an unequal number of patients between OSRI groups.

Our analysis showed that the hazard of deaths increased by 75% for each advance in the OSRI classification. This value is close to the corresponding value of a 91% increase obtained in the analysis of Balain *et al* [16]. In our series over 50% of the patients with an OSRI score of 1 were alive at the time of analysis. Those with an OSRI score of 7 had a median survival of just 58 days. Balain *et al* [16] found that patients with an OSRI score of 1 had a median survival of 23 months; those with a score of 7 had a median survival of just 1 month. This substantial difference is likely to prove useful in treatment making decisions for patients presenting with spinal metastases when surgical treatment is being considered. The OSRI is a user-friendly tool, as timely investigations to search for metastases; e.g. bone scans are not required to calculate the score.

The cross-validation procedure undertaken on the data set in the current analysis provides further support for the reliability of the OSRI score, with an expected small reduction of 6 percentage points in the proportion of cases correctly classified on the validation set as compared to the full data set.

Unlike the patients in the work of Balain *et al* [16], all patients in our study were treated surgically, therefore our survival figures relate to postoperative patients only.

Due to the use of the electronic patient record system, no patient was lost to follow-up, as dates of death were automatically entered on to the system. Hence censored data arises only from those patients remaining alive at the termination of the study.

One weakness of the study is the limited number of patients that were analysed. A larger study would have greater power to detect differences in survival between patients with different OSRI scores. Another potential limitation is that only surgical patients were included. This was because our unit is a tertiary referral centre and the majority of patients with MSCC not having surgery will remain at their local hospital for treatment rather than being transferred. However, the exclusion of non-surgical patients improves the internal validity of the study and precludes confounding by surgical status. In an optimal model those patients having radiotherapy should also be included.

Survival was defined from referral to our unit until date of death. An improvement could be made by determining the date of diagnosis of the primary tumour and calculating survival from then until death.
From our experience we can confirm the OSRI is a significant predictor of survival and is a useful tool when considering surgical treatment for patients with spinal metastases. The OSRI has demonstrated good transferability across data sets, self-consistency and predictive capability in a validated study. We recommend its use.

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