The Oswestry Spinal Risk Index (OSRI) in assessing prognosis of patients with spinal metastases

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ABSTRACT

Introduction: The Oswestry Spinal Risk Index (OSRI) was designed to predict life expectancy of patients presenting with spinal metastases. It integrates the most predictive items of existing scores and is calculated using not more than two items: General condition and primary tumor.

Research question: The purpose of this study was to externally validate the OSRI in a large cohort and to compare it with the established scores.

Material and methods: We retrospectively identified 211 consecutive surgical patients with symptomatic spinal metastases. We collected clinical and radiographic data, such as Karnofsky Performance Score (KPS), Frankel Status, primary tumor pathology and metastatic spread to calculate the Tokuhashi score, Tomita score, modified Bauer score and the OSRI. Logistic regression models, Kaplan-Meyer-curves, discriminant power and variance analyses were applied using Harrell's C-index and Cox and Snell's Pseudo R^2.

Results: Predicted and actual survival of our cohort's patients correlated significantly in each investigated scoring systems ($p < 0.001$). In test quality measurements Tokuhashi score performed best (C = 0.7204; R^2 = 0.3619), followed by OSRI (C = 0.7023; R^2 = 0.2612), Tomita (C = 0.6748; R^2 = 0.2818) and modified Bauer score (C = 0.6653; R^2 = 0.2486). Accuracy of predicted life expectancy was highest in modified Bauer score and OSRI.

Discussion and conclusion: Compared to the original scores, the OSRI provided equal or even superior results in assessing our study population's life expectancy. Its particular advantage lies in the simplicity of its application, which well meets the demands of surgical decision-making in daily practice.

1. Introduction

Spinal metastases account for the majority of neoplastic lesions of the skeletal system and the majority of spinal tumors (Aaron, 1994). With improving systemic therapies, life expectancy of tumor patients increases and consequently the incidence of spinal metastases. Aim of the surgical treatment of spinal metastases for most cases is symptom palliation, i.e. to reduce pain, preserve or restore spinal stability and neurological function and thereby the patients' quality of life (Berger, 2008). Furthermore, in some cases surgery has the additional aim to prepare for adjuvant radiosurgery by tumor separation from the spinal cord or for select cases to aim for a complete tumor resection. However, the possible morbidity and mortality of surgery and the burden of perioperative hospitalization must be balanced against the advantages of surgery, when counselling patients with limited life expectancy. Therefore, a reliable

assessment of risk factors and prognostic classifications of the course of the diseases and the expected survival time are of utmost importance in daily practice. A variety of patient- and disease-related parameters have been investigated for their prognostic value and were summarized into several scoring systems, intending to facilitate clinical decision-making. Among these the revised Tokuhashi score, Tomita score and the modified Bauer score are the most commonly applied tools (Leithner et al., 2008; Tokuhashi et al., 2005; Tomita et al., 2001). However, the prognostic relevance of these scores is weakened by newly evolving therapeutic approaches for certain tumor types and the assessment of prognosis and therapy is ideally defined by multidisciplinary team (MDT) boards.

But emergency situations require treatment decisions outside MDT and a scoring system is helpful. Most scores are hampered in practicability in emergency situations as many parameters of the score might not

be available upon acute neurological deficits when a treatment decision is necessary. The Oswestry Spinal Risk Index (OSRI) aims to overcome the limitation of practicability and usefulness in emergency situations. It integrates the most predictive items of the three well known scores – primary tumor type and Karnofsky Performance Score - and was designed to be a simple and practicable score, which offers valid information about patients' life expectancy (Balain et al., 2013). Since the OSRI has been validated poorly and life expectancy presents the core variable in clinical decision-making whether to intervene surgically or not (Choi et al., 2010; Pointillart et al., 2011), it is the purpose of this study to validate the OSRI in an external cohort by investigating its predictive value concerning patients' survival and to compare it with the established three scores, mentioned above.

2. Methods

The departmental database was retrospectively screened for patients undergoing surgical treatment for spinal metastases during a time period of 76 months. Metastases of solid primary tumors were included as well as solitary plasmocytomas and multiple myelomas. All patients treated surgically for their spinal metastatic disease were included. Patients lost to follow up and cases in which histological analyses remained uncertain were excluded. Relevant clinical data of the identified patients were gathered from patients' charts, earlier medical reports and the local tumor registry. For assessment of metastatic status of the disease, all available radiographic data were evaluated, comprising CT/MRI of the spine and whole body as well as PET/PET-CT examinations.

In all cases the preoperative revised Tokuhashi score, Tomita score, modified Bauer score and OSRI were calculated. Originally, Tokuhashi and Tomita scores were set up to evaluate metastases of solid tumors. However, the authors of OSRI and others showed statistical consistency of the scores when applied in myeloma cases (Leithner et al., 2008; Balain et al., 2013). Therefore, this group of frequently treated spinal tumors was included in our study. General health and neurological status of patients were assessed by means of KPS and Frankel score.

Statistical analyses were performed using SPSS® Version 22 and R Version 3.1.0 (R Foundation for Statistical Computing). Statistical significant differences were assumed at an error probability of $p \leq 0.05$.

3. Results

3.1. Baseline data

We identified 234 patients of which 23 were lost to follow up resulting in 211 patients that were analyzed. Of these, 150 were male and 61 female with a mean age of 68 years and a mean preoperative KPS of 70%. (Table 1).

Of 118 patients with a neurological deficit prior to surgery, the neurological status of 21 patients improved postoperatively. In 3 cases the postoperative Frankel score worsened. Fig. 1 gives an overview of the pre- and postoperative neurological status of patients' Frankel scores. In 149 (71%) cases the tumor staging revealed multi-focal spinal metastases. Extraspinal osseous metastases were present in 154 (73%) cases, additional visceral tumor manifestations in 90 (43%) cases. Table 2

Table 1
Overview of patient characteristics.

Characteristics	
Patients (n)	211
Male (n, %)	150 (71.1)
Female (n, %)	61 (28.9)
Mean (range) age (years)	68 (20–91)
Mean KPS (%)	70
80–100% (n)	89
50–70% (n)	99
10–40% (n)	24

outlines the primary tumor types of included patients.

Those tumor entities that occurred in less than 2.0% of cases were grouped as "other" category (n = 26; 12.3%). In the vast majority of cases (n = 196, 92.9%) surgical decision was made after preoperative case discussion by MDT comprising neurosurgical, radiological, oncological and radiation oncological expertise. In the rest of cases emergency situations required immediate decision making and the survival prognosis of patients was estimated after consultation of the respective specialist.

3.2. Survival

At time of evaluation 175 of the 211 patients had already died. Altogether, median survival time after surgery for spinal metastases was 9 months with a mean of 18.7 ± 1.6 months.

In log-rank analysis preoperative KPS' influence on survival was highly significant ($p < 0.001$) (Fig. 2).

Both pre- and postoperative Frankel scores of E were significant positive predictors for longer survival when compared to Frankel scores A – D ($p < 0.001$).

With regard to tumor entities, patients with spinal manifestation of multiple myeloma and breast cancer survived significantly longer than patients suffering from malignant melanoma, prostate, renal or lung cancer ($p < 0.001$) (Fig. 3.).

In the overall cohort the number of metastases along the spinal column showed a significant negative correlation with survival. Patients with one spinal lesion survived a mean of 26.9 months, with two lesions 21.1 months and with three or more spinal lesions 16.4 months ($p = 0.021$). In contrast, no significant impact on survival was observed in case of presence of extraspinal bone metastases ($p = 0.690$). However, the presence of resectable or not resectable visceral metastases at preoperative assessment was associated with a significantly shorter mean survival of 11.1 months and 7.3 months, respectively, compared to 26.2 months in the absence of visceral metastases ($p < 0.001$).

3.3. Validation of scores

3.3.1. Revised Tokuhashi score

Table 3 shows the predicted survival according to calculated revised Tokuhashi scores and the actual survival of the patients. The accuracy of predicted survival was best in the subgroup with favorable outcome of >1 year (81.1%). Among the other groups, prognostic power of the revised Tokuhashi score was poor with an overall accuracy in only 47.7%. Yet, correlation of shorter actual survival with increasing revised Tokuhashi score was highly significant ($p < 0.001$), Fig. 4.

3.3.2. Tomita score

Categorizing the patients according to Tomita resulted in a majority of 124 patients with slowly growing primary tumors, 121 patients without visceral metastases and 182 patients with multiple skeletal lesions (Table 4).

Table 5 shows the predicted and actual survival of patients as well as the proposed treatment according to Tomita score. Statistical analyses using the log-rank-test showed significant correlation of postoperative survival with prognostic groups ($p < 0.001$). Paired analyses of subgroups revealed significant longer and shorter survival of the best and worst subgroup, respectively, compared to the other groups. Difference in survival of the two middle subgroups was not significant ($p = 0.377$). Multivariate analyses found significant independent influence on average survival of all the three components of the Tomita score - kind of primary tumor and presence of visceral metastases ($p < 0.001$) as well as extension status of skeletal metastases ($p = 0.04$).

3.3.3. Modified Bauer Score

Tables 6 and 7 show the distribution of the prognostic factors among the study collective and the resulting scores according to the modified Bauer Score.
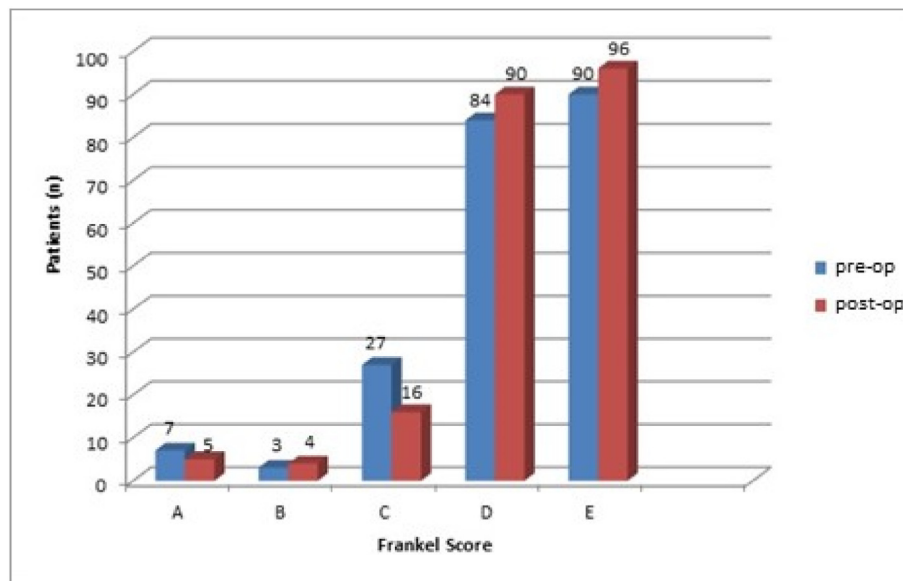
Fig. 1. Frankel scores pre- and postoperatively.

Table 2
Gender-specific frequency distribution of the primary tumors.

Primary tumor type	men (n = 150) n (%)	women (n = 61) n (%)	total (n = 211) n (%)
Prostate	53 (35,3)	–	53 (25,1)
Breast	1 (0,7)	30 (49,2)	31 (14,7)
Multiple myeloma	24 (16,0)	3 (4,9)	27 (12,8)
Lung	16 (10,7)	9 (14,8)	25 (11,8)
Kidney	17 (11,3)	5 (8,2)	22 (10,4)
Esophagus	7 (4,7)	1 (1,6)	8 (3,8)
Melanoma	6 (4,0)	1 (1,6)	7 (3,3)
Thyroid	4 (2,7)	3 (4,9)	7 (3,3)
Lymphoma	3 (2,0)	2 (3,3)	5 (2,4)
Others	19 (12,7)	7 (11,5)	26 (12,3)
Total	150 (100,0)	61 (100,0)	211 (100,0)
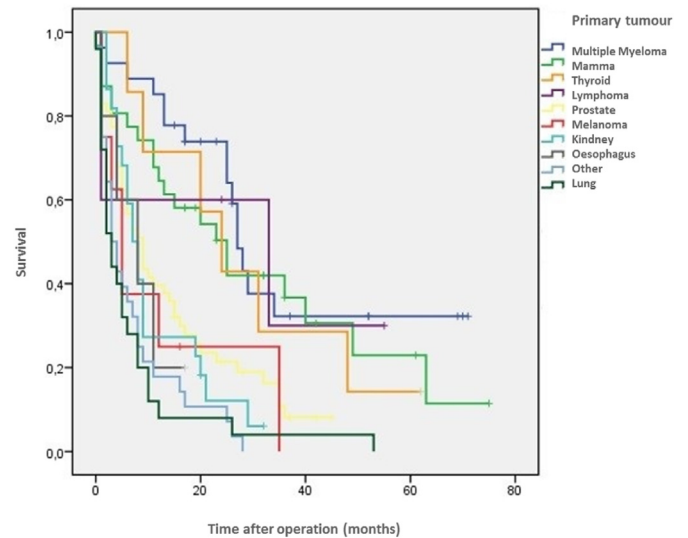
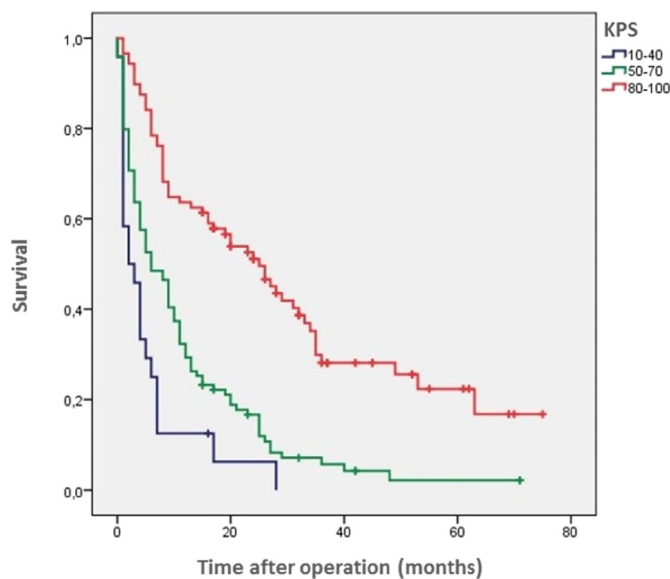**Fig. 3.** Survival curves for the different primary tumor subgroups.

Table 3
Predicted survival according to the modified Tokuhashi score and actual survival.

Tokuhashi score	Predicted survival acc. Tokuhashi	Patients n (%)	Actual survival		
			≤6 mo. n (%)	6–12 mo n (%)	≥ 12mo. n (%)
0–8	≤6 months	98 (46.4%)	**59** (60.2%)	19 (19.4%)	20 (20.4%)
9–11	6–12 months	76 (36.0%)	24 (31.6%)	11 (14.5%)	41 (53.9%)
12–15	≥12 months	37 (17.5%)	5 (13.5%)	2 (5.4%)	**30** (81.1%)

The absence of visceral metastases, no lung cancer and a primary tumor of breast, renal, lymphoma or myeloma had independent and significant influence on patients' survival in multivariate analyses (Table 6). The overall distribution of patients sorted by the subgroups of Modified Bauer score was significantly associated with survival (p < 0.001). Also did the paired analysis of the three subgroups show

Fig. 2. Survival curves of the subgroups of Karnofsky Performance Score (KPS).
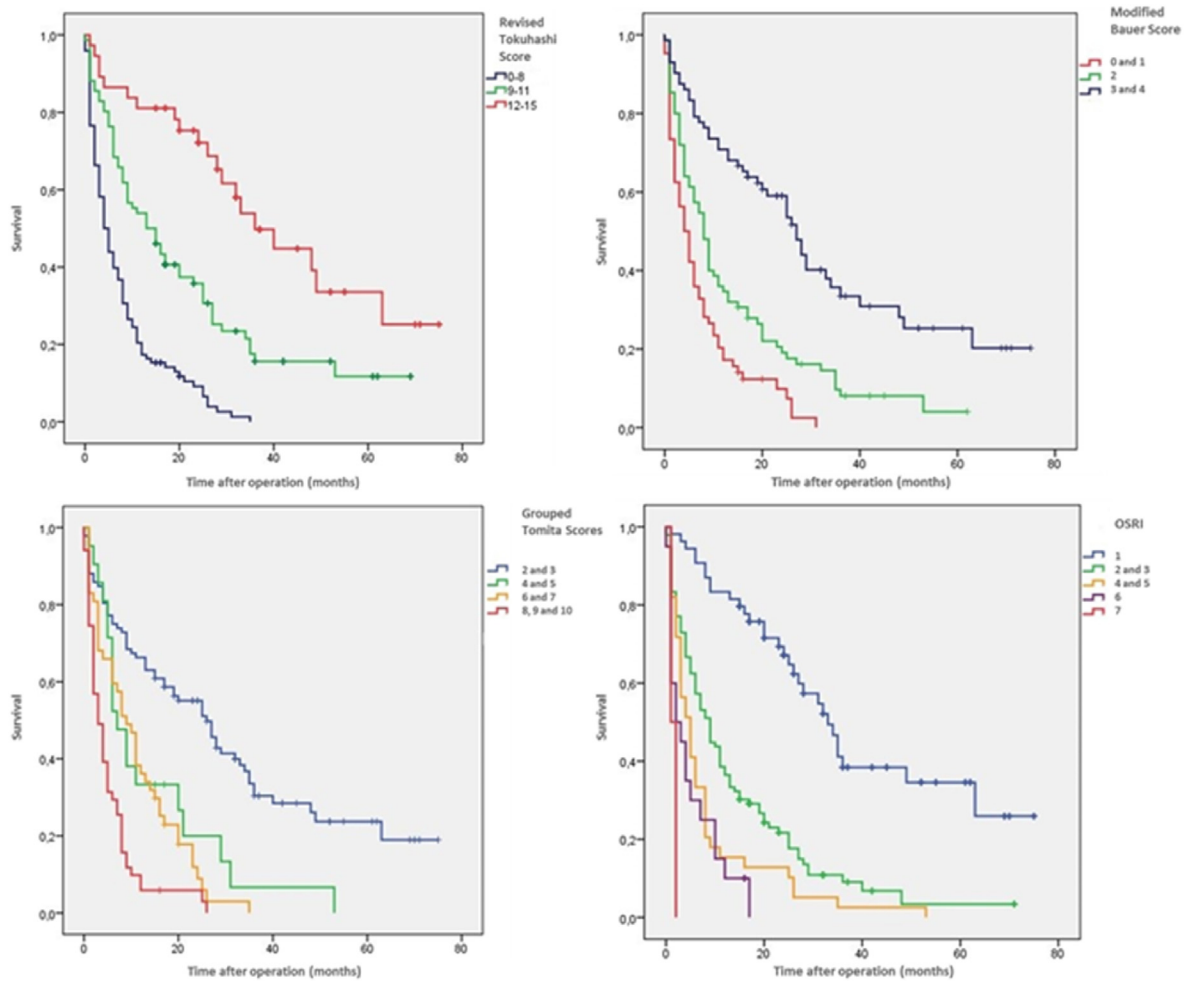
Fig. 4. Survival curves of the four assessed scores and their respective subgroups.

Table 4
Distribution of patients according to Tomita score.

Score	Prognostic factors					
	Primary tumor	Patients n (%)	Visceral metastases	Patients n (%)	Bone metastases	Patients n (%)
0	–	–	None	0	–	–
1	Slow growth (breast, thyroid, etc.)	124 (58.8%)	–	–	Solitary or isolated	29 (13.7%)
2	Moderate growth (kidney, uterus, etc.)	26 (12.3%)	Treatable	19 (9.0%)	Multiple	182 (86.3%)
4	Rapid growth (lung, stomach, etc.)	61 (28.9%)	Untreatable	71 (33.6%)	–	–

Table 5
Classification according to Tomita score, proposed treatment and actual survival of patients.

Tomita score	Patients n (%)	Predicted survival acc. Tomita in months	Proposed treatment	Actual average survival in months	p-value
2/3	92 (43.6%)	49.9	Excisional	31.0 ± 3.0	**< 0.001**
4/5	21 (10.0%)	23.5	Intralesional	14.1 ± 3.3	
6/7	47 (22.3%)	15	Palliative surg.	11.0 ± 1.3	
8/9/10	51 (24.2%)	5.9	Supportive	5.3 ± 0.8	

Table 6
Frequency distribution and statistical relevance of prognostic factors of the modified Bauer Score, *significance in multivariate analysis after Cox Regression Model.

Score	Prognostic factors	Patients n (%)	p – value (multivariate)
1	No visceral metastases	121 (57.3%)	<0.001*
1	No lung cancer	186 (88.2%)	0.028*
1	Primary = breast, kidney, lymphoma or myeloma	85 (40.3%)	0.02*
1	Solitary skeletal metastases	29 (13.7%)	0.07*

Table 7

Classification according to the modified Bauer score, proposed treatment goals, surgical strategy and actual survival of patients.

Modified Bauer score	Patients n (%)	Predicted mean survival acc. mod. Bauer in months	Treatment goal acc. mod. Bauer score	Proposed surgical strategy	Actual mean survival in months	p-value
0 and 1	64 (30.3%)	3 (0–5)	Supportive	No surgery	4 (2–6)	< **0.001**
2	75 (35.6%)	10 (2–18)	Short-term palliation	Dorsal surgery	8 (6–10)	
3 and 4	72 (34.1%)	30 (12–48)	Middle-term local control	Ventrodorsal surgery	27 (21–33)	

Table 8

Distribution of patients according to scoring items of OSRI.

Parameter	Score	Patients (n)
Primary tumor pathology (PTP)		
Slow growth **(breast, thyroid, prostate, myeloma, hemangioma, endothelioma, Non-Hodgkin-Lymphoma)**	1	124
Moderate growth **(renal, uterus, tonsil carcinoma, epipharynx carcinoma, synovial cell sarcoma, metastatic thymoma)**	2	26
Rapid growth **(stomach, colon, liver, melanoma, teratoma, sigmoid, pancreas, rectum, unknown)**<	4	36
Very rapid growth **(lung)**	5	25
General condition (GC)		
Poor (KPS 10–40%)	0	**24**
Moderate (KPS 50–70%)	1	**99**
Good (KPS 80–100%)	2	**88**

Table 9

Classification of patients according to OSRI, predicted and actual survival.

OSRI Score	Patients n (%)	Predicted mean survival acc. OSRI in months	Actual mean survival in months	p-value
1	54 (25.6%)	23 (12–36)	33 (27–39)	< **0.001**
2 and 3	96 (45.5%)	6 (4–9)	9 (7–11)	
4 and 5	39 (18.5%)	4 (3–5)	5 (3–7)	
6	20 (9.4%)	2 (1–3)	2 (0–5)	
7	2 (0.9%)	1 (1–2)	1	

significant differences in survival (p ≤ 0.003).

3.4. Oswestry Spinal Risk Index

The OSRI was calculated according to Balain et al.: PTP + (2-GC) (Balain et al., 2013) (PTP = Primary tumor pathology; GC = General condition). Distribution of the study population, classification of the OSRI subgroups and their average and mean survival are shown in Tables 8 and 9.

Association of the OSRI subgroups with actual survival was highly significant (p < 0.001). Paired comparison of the subgroups confirmed these findings for the groups of OSRI Score 1 and Score 2 and 3 (p < 0.001 and p ≤ 0.013). The group of OSRI Score 6 did not differ significantly in survival compared to the two adjoining groups. In multivariate analyses independent and highly significant influence of the two variables of OSRI on patients' survival was confirmed (p < 0.001).

3.5. Comparison of prognostic scores

3.6. Test quality measurements

To measure the ability of comparing survival of patients Harrell's C-

Table 10

C-indices and R^2 of the prognostic scores and of KPS. 95 %-confidence intervals of differences in C-indices of paired score analyses. *marks significance in difference.

Item	C-index	95 %-confidence interval	R^2
Tokuhashi (revised)	0.7204	0.6815–0.7596	0.3619
Tomita	0.6748	0.6326–0.7173	0.2818
Bauer (modified)	0.6653	0.6252–0.7065	0.2486
OSRI	0.7023	0.6637–0.7387	0.2612
KPS	0.6720		0.2315
		95 %-confidence interval of difference in C-index	
OSRI – Tokuhashi		- 0.0479–0.0125	
OSRI – Tomita		- 0.0083–0.0635	
OSRI – Bauer		- 0.0016–0.0764	
Tokuhashi – Tomita		0.0132–0.0767*	
Tokuhashi – Bauer		0.0234–0.0881*	
Tomita – Bauer		0.0208–0.0404	

index (Harrell et al., 1984) was calculated for each of the prognostic scores as well for KPS. A C-index of 1 means exact estimation of the survival of each individual of the analyzed collective. Best C-indices were reached by the revised Tokuhashi Score (0.7204) and the OSRI (0.7023) compared to lower C-indices of the Tomita (0.6748) and modified Bauer score (0.6653). The differences of C-indices of Tokuhashi and Tomita as well as Tokuhashi and Bauer Score were shown to be significant. With a C-index of 0.6720 KPS showed a comparable concordance of predicted and actual survival as Tomita and modified Bauer score.

Cox and Snell's Pseudo R^2 (Cox, 1972) was calculated for each regression model of the different scores quantifying the variance of survival attributable to the configuration of the system. Each score reached an R^2 of 0.2–0.4, which are classified as acceptable to good. Highest R^2 was reached in revised Tokuhashi score (0.3619), followed by Tomita (R^2 = 0.2818), OSRI (R^2 = 0.2612) and modified Bauer score (R^2 = 0.2486) (Table 10).

4. Discussion

We retrospectively analyzed a single center patient cohort that was treated surgically for symptomatic spinal metastatic disease. The purpose of this study was to externally validate the predictive power of the OSRI and to compare it with the established scores of Tomita, Tokuhashi and Bauer.

We found a highly significant correlation of prognosed and actual survival of patients for each of the investigated scores. In test quality analysis of the different scores, we found Tokuhashi score and OSRI to most accurately discriminate patients according to their score count and prognosed survival. In variance analysis each score reached acceptable to good results. Thus, in test quality measurements Tokuhashi score performed best, followed by OSRI, Tomita and modified Bauer score, which delivered comparable results. Yet, there are strengths and weaknesses of the single scores and their items, which are discussed below. But, OSRI is an useful tool to prognosticate patient survival with very basic

information readily available in most emergency situations.

Tokuhashi et al. found their revised score to accurately predict actual survival time in 82.5% of cases in the retrospective study arm and in 86.4% of cases in the prospective study arm (Tokuhashi et al., 2005).

Applying the revised Tokuhashi score to our cohort, it was capable of accurately prognosing the time of survival in months in 47.4% of cases, only, yielding differences in the single subgroups. These findings are in line with previously published data, suggesting that in light of improving oncological treatment modalities the revised Tokuhashi score tends to underestimate prognosis (Leithner et al., 2008; Gakhar et al., 2013; Quraishi et al., 2013).

Applied to our cohort, the Tomita Score provided prognoses of survival time, that significantly correlated with actual survival. Yet, the subgroup analyses revealed insufficient discrimination of the two middle groups (p = 0.377). Consequently, in our cohort application of the proposed surgical strategy (palliative surgery vs. intralesional/marginal surgery) could not have been recommended reliably.

Additionally and similar to our findings with the Tokuhashi score, the Tomita score did not precisely prognose the absolute survival in months, with the difference, that Tomita score overestimated the time of survival of our cohort's patients.

Compared to Tokuhashi and Tomita score the modified Bauer score, published in 2008 by Leithner et al. (2008), provided a quite accurate estimation of survival in our cohort with good discrimination between the different groups and significant and independent prediction of survival by its items primary tumor and absence of visceral metastases.

A general aspect of all the above-mentioned prognostic models is the fact, that they have been established on the basis of a specific patient cohort and its respective most predictive patient- and disease-related data, which formed the different items of the scores. The more specifically a score is tailored towards its original population, the more difficult it will be to transfer its good results to other collectives (Alonzo, 2009; Sciubba et al., 2007). Against this background the authors of the OSRI intended to integrate the most predictive items of already existing scores into a new tool, that would be reliably assessable in external populations. At the same time, they facilitated the score's composition by avoiding the use of redundant and in terms of predictive value inferior data. Thus, they only considered 2 items: primary tumor and general status by means of KPS (Balain et al., 2013). The advantages of the facilitated tool are its usability in daily clinical routine as the diagnosis of the primary tumor is usually ensured at time of detection of spinal metastases and the general status of a patient can be objectified by thorough anamnesis and clinical examination. By not considering the status of metastatic spread as the other scores do, the calculation of the OSRI does not require radiographic staging examinations, as they are frequently not available at point of surgical decision-making. This aspect makes the score especially useful in emergency situations where information on the stadium of the tumor disease is lacking and an interdisciplinary evaluation by a tumor board not possible.

Our findings of prognosed and actual survival are well in line with the results of Balain et al. and those of Fleming et al. who also performed a retrospective external validation of the OSRI (Balain et al., 2013; Fleming et al., 2016). Higher scores in OSRI where significantly correlated to shorter survival time. Solely the group of patients with most favorable prognosis lived comparably longer in our cohort (Tbl. 7). Both KPS and primary tumor were significant predictors of survival. The discriminant power of the two subgroups with 1 and 2 or 3 points was significant against all other groups. Similar results were previously found in another validation study of OSRI (Whitehouse et al., 2016). The discrimination of the subgroup with 6 points against the adjoining groups was not significant. The low number of patients in the subgroup with 7 points (n = 2) may take account for that.

As a potential selection bias we have to acknowledge, that we exclusively analyzed surgically treated patients with a certain survival prognosis according to initial multidisciplinary assessment. This may

have resulted in an underrepresentation of patients with poor prognosis of less than 6 months with an OSRI score ≥4. Nevertheless, we found nearly 1/3 of our patients to have survived less than 6 months following surgery, which should be considered in the context of highly individualized treatment decisions, when patients opt for surgery despite an advanced stage of the disease. With regard to this, the OSRI score provides a useful tool especially in emergency situations and high scores of ≥4 should clearly be discussed with patients and their families when individual expectations do not match prognosed survival.

5. Conclusion

In our study the OSRI's predictive and discriminant value was reliable and similar or even superior compared to further established scores. Considering its straightforward configuration, the OSRI provides a valid and practicable tool for spine surgeons in preoperative assessment of patients' survival time especially in emergency situation where more detailed patient information necessary for other scores or a tumor board decision is often lacking. Unlike other scores, the OSRI does not propose any surgical strategies, which, facing highly individualized oncological treatment concepts and personal as well as social circumstances of patients, seems to be an adequate approach for a modern scoring tool.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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