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External Validation and Optimization of the SPRING Model for Prediction of Survival After Surgical Treatment of Bone Metastases of the Extremities

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Abstract

Background Survival predictions before surgery for metastatic bone disease in the extremities (based on statistical models and data of previous patients) are important for choosing an implant that will function for the remainder of the patient's life. The 2008-SPRING model, presented in 2016, enables the clinician to predict expected survival before surgery for metastatic bone disease in the extremities. However, to maximize the model's accuracy, it is necessary to maintain and update the patient database to refit the prediction models achieving more accurate calibration.

Questions/purposes The purposes of this study were (1) to refit the 2008-SPRING model for prediction of survival before surgery for metastatic bone disease in the extremities with a more modern cohort; and (2) to evaluate the performance of the refitted SPRING model in a population-based cohort of patients having surgery for metastatic bone disease in the extremities.

Methods We produced the 2013-SPRING model by adding to the 2008-SPRING model (n = 130) a cohort of patients from a consecutive institutional database of patients who underwent surgery for bone metastases in the

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extremities with bone resection and reconstruction between 2009 and 2013 at a highly specialized surgical center in Denmark (n = 140). Currently the model is only available as the nomogram fully available in the current article, which is sufficient to use in daily clinical work, but we are working on making the tool available online. As such, the 2013-SPRING model was produced using a consecutive cohort of patients (n = 270) treated during an 11-year period (2003-2013) called the training cohort, all treated with bone resection and reconstruction. We externally validated the 2008-SPRING and the 2013-SPRING models in a prospective cohort (n = 164) of patients who underwent surgery for metastatic bone disease in the extremities from May 2014 to May 2016, called the validation cohort. The validation cohort was identified from a cross-section of the Danish population who were treated for metastatic lesions (using endoprostheses and internal fixation) in the extremities at five secondary surgical centers and one highly specialized surgical center. This cross-section is representative of the Danish population and no patients were treated outside the included centers as a result of public healthcare settings. The indications for surgery for training and the validation cohort were pathologic fracture, impending fracture, or intractable pain despite radiation. Exact date of death was known for all patients as a result of the Danish Civil Registration System and no loss to followup existed. In the training cohort, 150 patients (out of 270 [56%]) and in the validation cohort 97 patients (out of 164 [59%]) died of disease within 1 year postoperatively. The 2013 model did not differ from the 2008 model and included hemoglobin, complete fracture/impending fracture, visceral and multiple bone metastases, Karnofsky Performance Status, and the American Society of Anesthesiologists score and primary cancer. The models were evaluated by area under the receiver operating characteristic curve (AUC ROC) and Brier score (the lower the better).

Results The 2013-SPRING model was successfully refitted with a cohort using more patients than the 2008-SPRING model. Comparison of performance in external validation between the 2008 and 2013-SPRING models showed the AUC ROC was increased by 3% (95% confidence interval [CI], 0%-5%; p = 0.027) and 2% (95% CI, 0%-4%; p = 0.013) at 3-month and 6-month survival predictions, respectively, but not at 12 months at 1% (95% CI, 0%-3%; p = 0.112). Brier score was improved by -0.018 (95% CI, -0.032 to -0.004; p = 0.011) for 3-month, -0.028 (95% CI, -0.043 to -0.0123; p < 0.001) for 6-month, and -0.014 (95% CI, -0.025 to -0.002; p = 0.017) for 12-month survival prediction.

Conclusions We improved the SPRING model's ability to predict survival after surgery for metastatic bone disease in the extremities. As such, the refitted 2013-SPRING model gives the surgeon a tool to assist in the decision-making of a surgical implant that will serve the patient for the remainder of their life. The 2013-SPRING model may provide increased quality of life for patients with bone metastasis because potential implant failures can be minimized by precise survival prediction preoperatively and the model is freely available and ready to use from the current article.

Level of Evidence Level I, diagnostic study.

Introduction

Estimating survival after surgical treatment of metastatic bone disease in the extremities is important for aiding the surgeon in determining the most reasonable treatment option for a patient with a pathologic fracture or an impending fracture. It is well established that the main goal is to choose an implant that will function for the remaining time of the patient's life. Patients who are expected to have a long survival after surgery would be better served by durable implants such as tumor prostheses rather than internal fixation to minimize the risk of implant breakage or nonunion [3, 7, 13].

A survey of Musculoskeletal Tumor Society members [23] revealed that 6-month postoperative survival was considered an indication for using a more durable implant in treatment of metastatic lesions of the proximal femur. If patients are expected to live more or less than 6 months, the surgeon should evaluate the gain of fast recovery against the risk of implant failure for individual patients. However, one study showed that a metastatic lesion cannot be expected to heal, even under treatment with radiotherapy and chemotherapy within the first 6 months after surgery [9]. When assessing a metastatic lesion in patients with a life expectancy < 6 months, we believe surgeons must consider the following: should the lesion be resected and the bone reconstructed with an artificial joint or a tumor-prosthesis as part of palliative pain control or would the patient be better off by stabilizing the lesion with internal fixation? Taking this into consideration, a survival prediction model should be able to estimate survival for multiple endpoints and not just 6 months. Furthermore, surgeons' subjective estimates of residual life expectancy can be overly optimistic [11]. This strengthens the importance of a clinical tool to predict life expectancy after surgery for metastatic bone disease in the extremities. Chen et al. [4] found small amounts of modern data to be more effective than large amounts of "old" data when producing prediction models for various clinical outcomes. In 2016, we proposed the 2008-SPRING model [22] to predict survival before surgery for metastatic bone disease in the extremities, a freely available tool.

We wanted to update the SPRING model with a more modern cohort and more patients to improve the SPRING

model's accuracy of present-day patients producing an improved clinical tool for decision-making.

Therefore, the purposes of this study were to (1) refit the 2008-SPRING model for predicting survival before surgery for metastatic bone disease in the extremities with a modern cohort; and (2) evaluate the performance of the refitted SPRING model in a population-based cohort of patients having surgery for a metastatic lesion in the extremities.

Patients and Methods

The SPRING Model

Proposed by this research group in 2016 [19], the 2008-SPRING model predicts survival 3, 6, and 12 months after surgery for metastatic bone disease in the extremities. We used a logistic regression model to build the model with data from a cohort of 130 patients who had joint replacement surgery from 2003 to 2008 (patients who were included in the early cohort of the COpenhagen BOne Metastasis database [COBOM] database [12]). We presented the model as three nomograms, one for each endpoint (survival at 3, 6, and 12 months after surgery for metastatic bone disease in the extremities).

Experimental Overview

Initially the statistical analysis forming the 2008-SPRING model was run using the early cohort of the COBOM database. In the current study, we combined the early and late cohorts of the COBOM database (n = 270) into a training cohort that produced the nomograms that form the 2013 model for prediction of survival after surgery for metastatic lesions in the extremities. The 2013-SPRING's performance was tested in an independent external cohort (called the validation cohort) formed in a prospective multicenter population-based study (Fig. 1). It was a predefined choice not to explore or include other variables into the 2013-SPRING model than used in the 2008-SPRING model (includes no data-driven selection).

Before study initiation, we obtained ethical approval from the regional ethic committee (ID no. H-4-2014-005) and institutional data protection agency (ID no. 30-1222).

Training Cohort (COBOM cohort)

The COBOM database [12] is an institutional database containing prospectively collected data of patients having bone resection and reconstruction for metastatic bone disease of the extremities at the Musculoskeletal Tumor Section, Rigshospitalet. Institutional policy is bone resection and reconstruction using endoprostheses/tumor prostheses or intercalary spacers after multidisciplinary evaluation and only rarely an internal fixation method is used (because we found a high failure rate as a result of implant wear-out). It was chosen not to include patients treated for metastatic lesions using an internal fixation method because consecutive registration of these patients has not been kept, and including them would increase the risk of selection bias of patients who were treated as a result of failed devices (selection of long-term survivors). In general, patients are candidates for surgical treatment in situations of pathologic fracture, impending fracture, or intractable painful lesions that cannot be managed by palliative measures (medication or radiation).

The database consists of an early cohort of patients treated from 2003 to 2008 before introduction of electronic patient records and a late cohort (2009-2013) after introduction of electronic patient records. Data from the early cohort (n = 130) were used to produce the 2008-SPRING model, whereas the complete database was used in the current study to produce the 2013-SPRING model (n = 270).

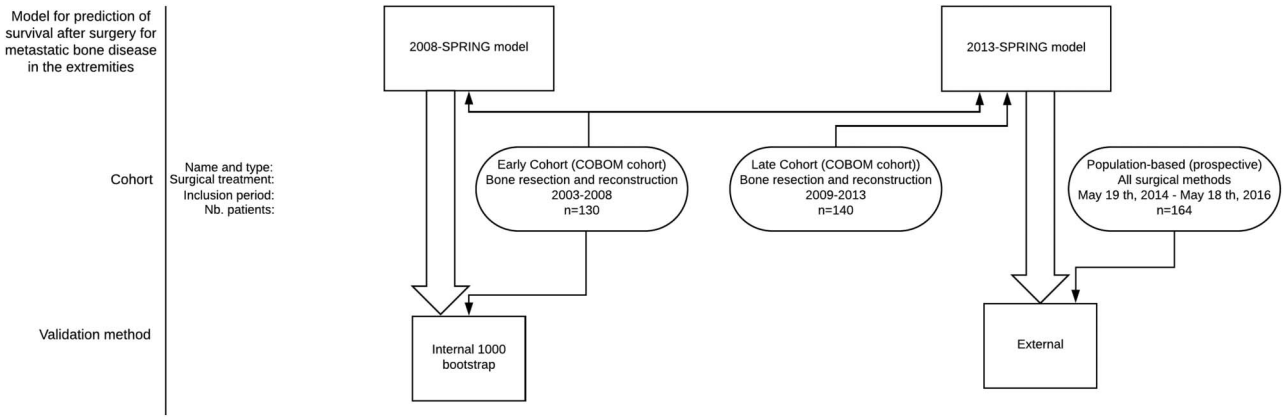

Fig. 1 Figure illustrating the distribution of cohort into the 2008-SPRING model and 2013-SPRING model and validation method.

Validation Cohort

The goal of this prospective, population-based cohort study (unpublished work Sørensen et al.) was to identify the incidence and epidemiologic composition of patients undergoing surgical intervention for metastatic bone disease in the extremities in the capital region of Denmark. The study identified 175 lesions treated in 164 patients (living in the region) from May 19, 2014, to May 18, 2016, at one of six centers (five secondary surgical centers and one highly specialized center). This region is a representable cross-section of the Danish population. As a result of a government-paid healthcare setting, all patients living in the region in need of treatment for metastatic bone disease will be treated at one of these six centers, and therefore no patient is lost to inclusion. All surgical treatment modalities were used in the cohort, and the study was purely observational and therefore no influence on treatment was present. In the validation cohort, 162 participants had a complete data set and were included for further analysis (because no imputation of missing data was performed, patients with missing data were excluded from analysis).

Followup

All patients had complete 12-month followup as a result of the Danish Civil Registration System [21] and precise date of death is known for all patients. No patients died from other reasons than the primary malignancy ensuring no competing risk. In the training cohort, 150 patients (out of 270 [56%]) and in the validation cohort 97 patients (out of 164 [59%]) died of disease within 1 year after surgery. The median potential followup time since surgery of our study was 61 months (interquartile range [IQR], 33-126). The median time to death since surgery in our cohort was 8 months (IQR, 2-30). In the validation cohort, potential median followup time was 30 months (IQR, 20-34) and median time to death 8 months (IQR, 2-28). In the training cohort, potential median followup time since surgery was 103 months (IQR, 70-131). Median time to death since surgery in the training cohort was 9 months (IQR, 2-32).

Variables

Variables included in the 2013-SPRING model did not differ from the original 2008-SPRING model and included hemoglobin, impending/or complete fracture of lesion, visceral metastases (if no preoperative scans were performed, status of surveillance scans performed up to 3 months postoperatively were considered as baseline scans), multiple bone metastases (same approach as visceral metastasis), Karnofsky Performance Status (KPS; ≥ 70 or < 70), and the American Society of Anesthesiologists score (ASA; 1 + 2 or 3 + 4). We categorized the primary cancer as slow-, moderate-, and fast-growing depending on observed survival as described by Sørensen et al. [22]. We added "other cancers" to the fast-growing type, enabling clinicians to score cancers that rarely present with bone metastasis (Table 1).

Table 1. Grouping of primary cancers into prognostic groups

Prognostic group	Primary cancers
Fast-growing	Bladder, colorectal, hepatocellular, lung, malignant melanoma, unknown, others
Moderate-growing	Prostate, renal, sarcoma
Slow-growing	Breast, lymphoma, myeloma

When we compared the training cohort with the validation cohort, we observed no difference in the distribution of variables except for ASA, which was higher for the validation cohort (Table 2).

Statistics

The survival chances were predicted for individual patients at 3, 6, and 12 months after surgery using separate logistic regression models for the three prediction horizons. We evaluated the predictive performance of the models in the validation cohort using Brier score [2], area under the curve (AUC) of receiver operating characteristic (ROC) curves, and calibration plots.

The Brier score is the quadratic distance between the predicted survival probability (a value between 0 and 1) and the vital status at the prediction horizon (0 when the patient has died and 1 when the patient has survived). We reported the average Brier score in the validation cohort; lower scores are considered better. The AUC ROC is the probability that a randomly chosen patient who died before the prediction horizon received a lower survival chance with the SPRING model than a randomly chosen patient who survived until the prediction horizon. Furthermore, we present calibration plots. AUC ROCs were compared with the Delong-Delong test [6]. Brier scores were compared with Wald confidence intervals and a corresponding test based on the SD of the paired residuals.

No imputation of missing data was performed.

The level of statistical significance was set at 5%.

Results

Refiiting of the 2008-SPRING Model

The model was successfully refitted using the training cohort (complete COBOM database including all data from 2003 to 2013, n = 270) and presented in nomograms for the three

Table 2. Distribution and comparison of baseline variables between training and validation cohorts

Variable	Level	Training (n = 270)	Validation (n = 164)	Total (n = 434)	p value
Primary cancer growth	Slow	116 (43)	61 (37)	177 (41)	
	Moderate	70 (26)	51 (31)	121 (28)	
	Fast	84 (31)	52 (32)	136 (31)	0.402
Hemoglobin (mM)	Mean (SD)	7.3 (1)	7.2 (1)	7.2 (1)	0.367
	Missing	1	0	1	
Fracture	Impending fracture	72 (27)	41 (25)	113 (26)	
	Fracture	198 (73)	123 (75)	321 (74)	0.787
Visceral metastases	No	165 (61)	97 (59)	262 (60)	
	Yes	105 (39)	67 (41)	172 (40)	0.761
Multiple bone metastases	No	91 (34)	43 (26)	134 (31)	
	Yes	179 (66)	121 (74)	300 (69)	0.126
Karnofsky score	< 70	97 (36)	60 (37)	157 (36)	
	≥ 70	171 (64)	104 (63)	275 (64)	1.000
	Missing	2	0	2	
ASA group	1 + 2	137 (53)	67 (41)	204 (48)	
	3 + 4	124 (45)	95 (59)	219 (52)	0.033
	Missing	9	2	11	

Numbers in parentheses represent percent of total; ASA = American Society of Anesthesiologists.

prediction horizons (survival 3, 6, and 12 months after surgery; yes/no) (Fig. 2), nomograms that are freely available in presented form and ready to use in clinical settings. In the training cohort, all variables were associated with the odds of survival at all three endpoints except for the moderate-growing cancer group (odds ratio [OR], 1.95; 95% confidence interval [CI], 0.84-4.50; p = 0.118), multiple bone metastases (OR, 1.89; 95% CI, 0.89-4.04; p = 0.099), and the ASA score (OR, 1.91; 95% CI, 0.98-3.72; p = 0.057) at the 3-month endpoint. Fracture was not associated with changes in odds of survival outcome at any endpoint (3 months: OR, 1.43, 95% CI, 0.67-3.06, p = 0.354; 6 months: OR, 1.60, 95% CI, 0.78-3.28, p = 0.203; 12 months: OR, 0.68, 95% CI, 0.33-1.43, p = 0.313). OR for survival status at 3 months was highest for the presence of visceral metastasis (OR, 3.10; 95% CI, 1.62–5.93; p < 0.001) followed by fast-growing cancer (OR, 2.75; 95% CI, 1.26–6.03; p < 0.001). At 6 months, fast-growing cancer had the highest OR (OR, 7.01; 95% CI, 3.18–15.46; p < 0.001) followed by the presence of visceral metastasis (OR, 2.40; 95% CI, 1.27–4.56; p = 0.007). At 12 months, fast-growing cancer and the presence of visceral metastasis likewise have the highest OR (OR, 9.93; 95% CI, 4.29–22.98; p < 0.001 and OR, 2.47; 95% CI, 1.26–4.86; p = 0.008, respectively) (Table 3).

Evaluation of the Refitted 2013-SPRING Model in a Population-based Cohort (external validation)

AUC ROC in the external validation for survival prediction was 82% (95% CI, 73%–91%) at 3 months, 85% (95% CI, 76%–93%) at 6 months, and 86% (95% CI, 77%–95%) at 12 months (Fig. 3). The accuracy estimated by Brier score for survival prediction was 0.155 (95% CI, 0.121–0.188) at 3 months, 0.162 (95% CI, 0.127–0.198) at 6 months, and 0.152 (95% CI, 0.117–0.187) at 12 months.

The null model (prediction of the prevalence of mortality in the cohort without using the variables, the so-called "insanity test") yielded a Brier score of 0.220 (95% CI, 0.195–0.245) at 3 months, 0.246 (95% CI, 0.237–0.256) at 6 months, and 0.240 (95% CI, 0.225–0.255) at 12 months, resulting in an improvement in Brier score for prediction outcome by using the 2013-SPRING model compared with the null model of -0.066 (95% CI, -0.100 to -0.032; p < 0.001) for 3-month predictions, -0.084 (95% CI, -0.121 to -0.047; p < 0.001) for 6-month prediction, and -0.088 (95% CI, -0.124 to -0.052; p < 0.001) for 12-month prediction.

In comparison, the 2008-SPRING model preformed an AUC ROC of 79% (95% CI, 70%–88%) at 3 months, 82% (95% CI, 74%–91%) at 6 months, and 85% (95% CI, 76%–94%) at 12 months in external validation using the same validation cohort. The Brier score was 0.173 (95% CI, 0.135–0.210) at 3 months, 0.190 (95% CI, 0.146–0.235) at 6 months, and 0.166 (95% CI, 0.123–0.209) at 12 months. Comparison of AUC ROC and Brier score between the 2008-SPRING model and the 2013-SPRING model showed better performance of the refitted 2013 model with an increase in AUC ROC by 3% (95% CI, 0%-5%; p = 0.027), 2% (95% CI, 0%-4%; p = 0.013), and 1% (95% CI, 0%-3%; p = 0.112) at 3-, 6-, and 12-month survival predictions. Brier score was improved

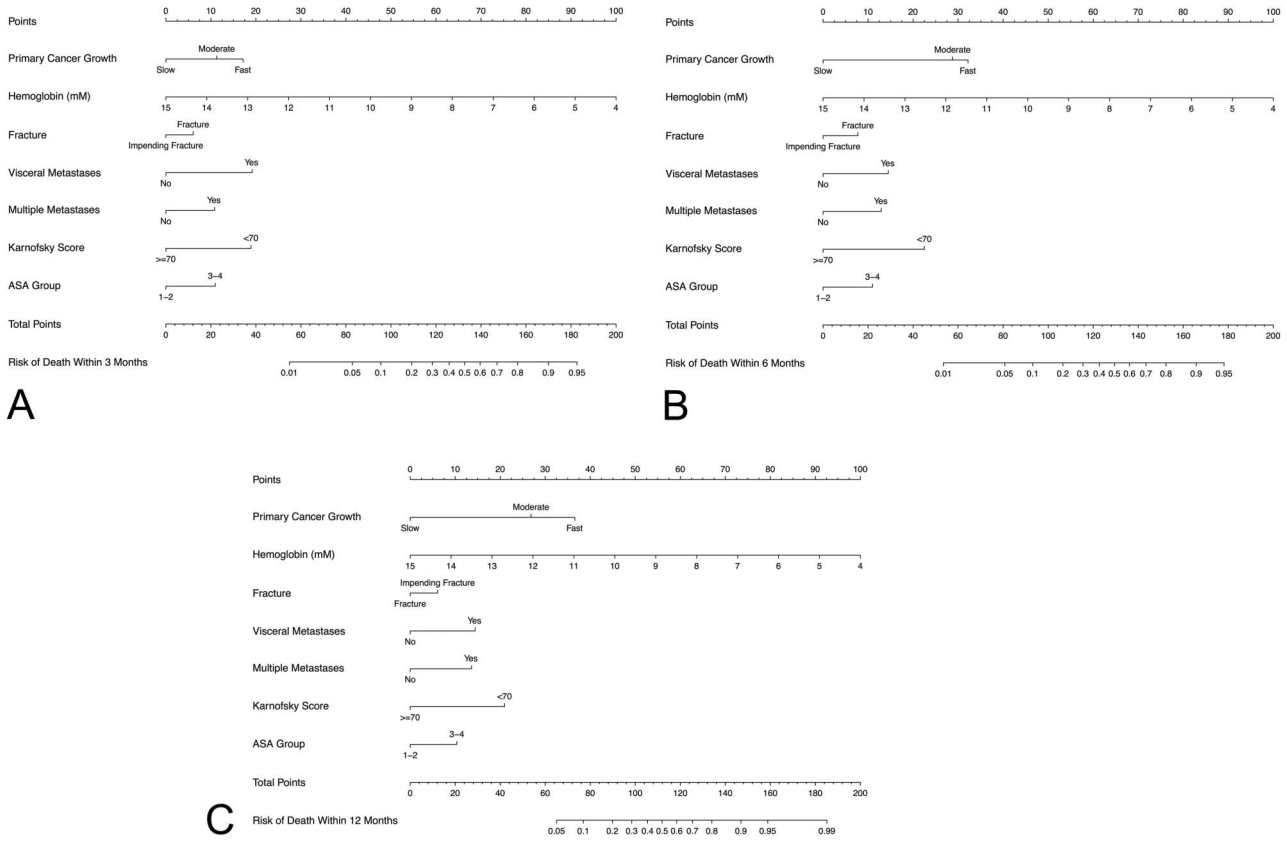

Fig. 2 A-C Figure showing the nomograms for prediction of survival 3 (**A**), 6 (**B**), and 12 (**C**) months after surgery for metastatic bone disease in the extremities. A patient is scored preoperatively on all variables. The sum of the variables correlates with the risk of death at the specific nomogram's endpoint (3, 6, or 12 months postoperatively).

in the 2013-SPRING model compared with the 2008 model by -0.018 (95% CI, -0.032 to -0.004; p = 0.011) for 3-month, -0.028 (-0.043 to -0.0123; p < 0.001) for 6-month, and -0.014 (95% CI, -0.025 to -0.002; p = 0.017) for 12-month survival prediction.

The model seemed well calibrated at all three endpoints (3, 6, and 12 months) in calibration plots (Fig. 4).

Discussion

Accurate survival predictions in patients undergoing surgery for metastatic bone disease in the extremities are important in providing a surgical treatment that will function for the patient's residual lifetime. As Chen and Asch [5] emphasize, even with the knowledge that a clinician tends to overestimate residual survival by a factor of 3, the combination of a clinical prediction model and the best human "hardware" will outperform either of these two scenarios alone. Taking this into consideration, creators of prediction models are obliged to constantly refit and improve such prediction models [4]. As such, we successfully refitted our SPRING model for predicting survival in patients undergoing surgery for metastatic bone disease in the extremities with a more modern cohort and more patients. We found that the refitted 2013-SPRING model's performance in an external population-based cohort of patients without selection of implant method was improved compared with the 2008-SPRING model.

The 2013-SPRING model is free to use and can be used directly from nomograms presented in the current article.

Our current study has few limitations because all three cohorts were consecutively enrolled and none were lost to followup. In addition, validation was performed on a population-based, prospective cohort of patients treated by both bone resection and reconstruction (endoprosthesis) and internal fixation. However, the SPRING model has been built on a solely Scandinavian population cohort, and as a result, discrepancies in indications for surgical treatment of metastatic bone disease worldwide may not be captured by this study where indication/threshold for surgery may differ from the current study. Validation of the 2013-SPRING model in a non-Scandinavian population is thus pending. Lastly, stratification for histogenesis of primary cancer is not accounted for in the SPRING model.

Table 3. Variables explaining the relation to survival outcome as expressed by multivariate logistic regression

		3-month survival			6-month survival			12-month survival		
Variable	Units	Odds ratio	95% CI	p value	Odds ratio	95% CI	p value	Odds ratio	95% CI	p value
Primary cancer group	Slow	1.00	1.00–1.00	1.000	1.00	1.00–1.00	1.000	1.00	1.00–1.00	1.000
	Moderate	1.95	0.84–4.50	0.118	5.69	2.50–12.93	< 0.001	5.39	2.41–12.06	< 0.001
	Fast	2.75	1.26–6.03	0.011	7.01	3.18–15.46	< 0.001	9.93	4.29–22.98	< 0.001
Hemoglobin		0.58	0.41–0.84	0.004	0.58	0.40–0.83	0.003	0.57	0.39–0.81	0.002
Fracture	Impending fracture	1.00	1.00–1.00	1.000	1.00	1.00–1.00	1.000	1.00	1.00–1.00	1.000
	Fracture	1.43	0.67–3.06	0.354	1.60	0.78–3.28	0.203	0.68	0.33–1.43	0.313
Visceral	No	1.00	1.00–1.00	1.000	1.00	1.00–1.00	1.000	1.00	1.00–1.00	1.000
	Yes	3.10	1.62–5.93	< 0.001	2.40	1.27–4.56	0.007	2.47	1.26–4.86	0.009
Multiple bone metastases	No	1.00	1.00–1.00	1.000	1.00	1.00–1.00	1.000	1.00	1.00–1.00	1.000
	Yes	1.89	0.89–4.04	0.099	2.19	1.07–4.48	0.032	2.35	1.13–4.89	0.022
Karnofsky status	< 70	1.00	1.00–1.00	1.000	1.00	1.00–1.00	1.000	1.00	1.00–1.00	1.000
	≥ 70	0.33	0.17–0.62	< 0.001	0.26	0.13–0.49	< 0.001	0.27	0.13–0.54	< 0.001
ASA score	1 + 2	1.00	1.00–1.00	1.000	1.00	1.00–1.00	1.000	1.00	1.00–1.00	1.000
	3 + 4	1.91	0.98–3.72	0.057	1.94	1.03–3.68	0.042	1.92	0.98–3.73	0.055

CI = confidence interval; ASA = American Society of Anesthesiologists.

This may lead to overly optimistic survival prediction for more aggressive histogenesis cancer such as, eg, epidermal growth factor receptor-positive lung cancer or hormone-resistant prostate cancer.

Previously several risk factors for survival in patients undergoing surgery for metastatic bone disease have been identified [8, 10, 14-16, 18]. Like other studies, our study did not show an influence of complete fracture compared with impending fracture [14-16, 18] on survival at any endpoint. Fracture does, however, seem to influence residual survival, according to data from randomized controlled trials of zoledronic acid [20]. Therefore, we still advocate that this variable should be considered when estimating residual life expectancy in patients with metastatic bone disease.

We included performance status in our prediction model measured with the ASA score and the KPS because these variables capture different aspects of performance. Anesthesiologists evaluate the ASA score preoperatively, and the score is strongly influenced by comorbidity and the anesthesiologist's subjective evaluation of risk of death [1], whereas the KPS evaluates a patient's ability to care for him- or herself. The KPS is comparable to the Eastern Cooperative Oncology Group (ECOG) level [17], which has previously been shown to predict residual survival after surgery for metastatic bone disease [15, 16, 18]. Our study indicates that both performance systems are important factors for predicting survival in patients with metastatic bone disease undergoing surgery, although KPS seems to outperform the ASA score in short-term survival. Lastly, we chose to include hemoglobin as a continuous factor rather than dichotomized into two or more groups [8, 10, 14, 16]. This seemed relevant, because no consensus of a clinical relevant cut has been established. Also, dichotomizing a variable can result in loss of power and residual confounding of outcome [19].

Our analysis showed an improvement in the SPRING model's ability to predict survival outcome after including a larger sample size of more modern patient material into the statistical analysis forming the prediction model. This is expected; Chen et al. [4] have established that more modern material will outperform a large quantity in model performance. This could explain why the 2013-SPRING model seems to outperform other prediction models for survival built on large data sets. Also, other models are sometimes built on populations identified from billing codes and as a result are vulnerable to selection bias, whereas our cohort is consecutive.

As a result, the 2013-SPRING model can assist the surgeon in choosing an implant that should serve the patient for their residual lifetime. As an example, a patient is scored to a 90% risk of death within 3 months after surgery

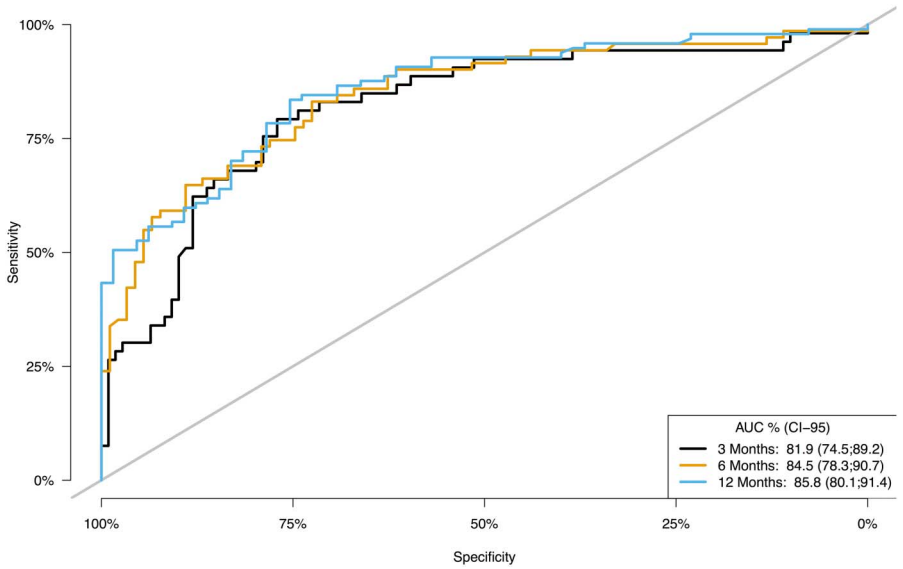

Fig. 3 Curves showing the ROC curves of the 2013-SPRING model at each endpoint (survival status 3 (black), 6 (yellow), or 12 (blue) months after surgery for metastatic bone disease in the extremities. AUC ROC of the refitted 2013-SPRING model was 82% (95% CI, 73%–91%) at 3 months, 85% (95% CI, 76%–93%) at 6 months, and 86% (95% CI, 77%–95%) at 12 months.

and may be best treated for a metastatic lesion in the trochanteric area with an intramedullary nail, because this patient most likely will not experience failure of the implant within 3 months. On the other hand, a patient who is scored a 10% risk of death within 12 months after surgery may be best treated for the very same lesion by wide bone resection and reconstruction with a tumor-prosthesis, because one cannot expect the lesion to heal, and as such, the use of an internal fixation method would lead to failure of the implant and revision surgery.

In conclusion, we were able to refit and improve the SPRING model to predict survival in patients having surgery for metastatic bone disease, providing the surgeon with an improved tool for residual life estimation, thus

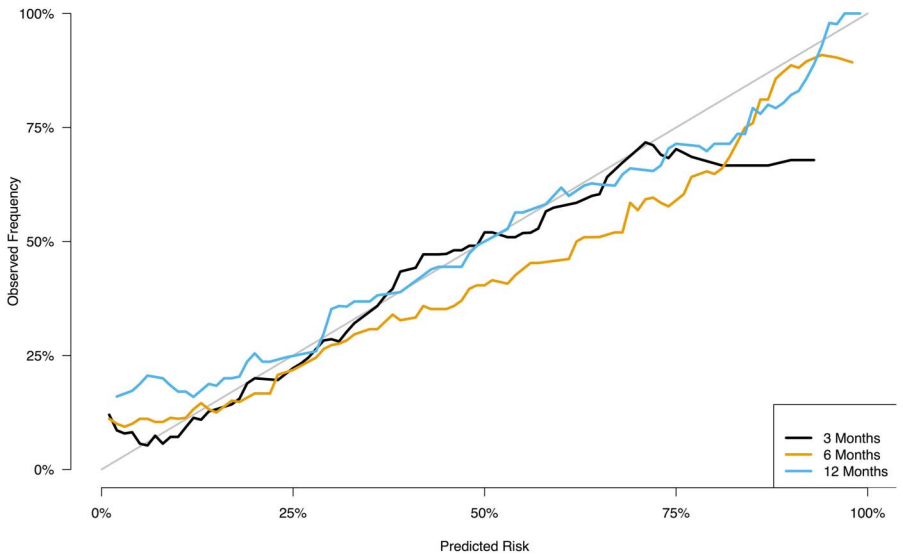

Fig. 4 Plots showing the calibration of the model at each survival endpoint after surgery for metastatic bone disease in the extremities: 3 months (black), 6 months (yellow), or 12 months (blue).

minimizing the risk of implant failure resulting from wear-out in long-term survivors. Also, we have proved that the performance of the SPRING model is accurate in a non-related and unselected cohort of patients treated with both endoprostheses and internal fixation. We present the refitted 2013-SPRING model for prediction of survival after surgery for metastatic lesions in the extremities as a nomogram for the first time in the current article. The 2013-SPRING model for predicting survival before surgery can be used freely from the nomograms provided in the current article.

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