Research Paper

External validation of a genitourinary cancer-specific prognostic scoring system to predict survival for patients with bone metastasis (modified B-FOM scoring model): Comparison with other scoring models in terms of accuracy

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ABSTRACT

Objective: We previously developed genitourinary (GU) cancer-specific scoring system for prediction of survival in patients with bone metastasis (the Bone-Fujimoto-Owari-Miyake [B-FOM] scoring model) based on five prognostic factors: the type of primary tumor (prostate cancer (PCa) vs renal cell carcinoma (RCC) and PCa vs urothelial carcinoma (UC)), poor performance status (PS), visceral metastasis, high Glasgow-prognostic score (GPS), elevated neutrophil-to-lymphocyte ratio (NLR). The aim of this study was to externally validate and further improve the performance of the B-FOM score.
Methods: The external validation cohort comprised 309 patients with GU cancer with bone metastasis from multiple institutions. Clinical factors were analyzed using Kaplan-Meier method and COX regression hazard model. Performance of a modified B-FOM score was compared to that of other scoring models by the Kaplan-Meier method and the area under the curve (AUC) of receiver operating characteristic curves.
Results: The median follow-up period of development and validation cohort were 25 and 17 months, respectively. Kaplan-Meier curve demonstrated that the type of primary tumor (RCC and UC vs PCa), poor PS, presence of visceral metastasis, high GPS, elevated NLR were significantly associated with shorter cancer-specific survival. Risk groups were successfully stratified by the modified B-FOM score classification. Moreover, the AUC of the modified B-FOM scoring model for predicting mortality at 6, 12, and 24 months were 0.895, 0.856, and 0.815, respectively, which were the highest among evaluated models.
Conclusions: The B-FOM scoring model is a simple and accurate prediction tool. By using this scoring model at the time of the diagnosis of bone metastasis in patients with GU cancers, an individualized optimal treatment strategy can be selected.

1. Introduction

Accurately predicting the prognosis of individual patients with genitourinary (GU) cancer with bone metastasis (BM) is essential for clinical physicians (including urologists, orthopedic surgeons,

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and radiation oncologists) to determine an optimal treatment strategy [1]. Treatment strategies for patients with GU cancer with BM have been recently verified [2–4]. The main treatment strategies for patients with BM comprise bone modifying agents, such as zoledronic acid or denosumab [5], opioid analgesics, and palliative radiotherapy [6], which can improve the patient's quality of life by preventing skeletal-related events and relieving bone pain BM. However, the efficacies of several aggressive approaches, such as a higher dose or longer course of curative radiation therapy, and surgical interventions for local tumor lesions have been demonstrated [7–9]. Therefore, if a patient is expected to have a longer survival based on highly accurate prognosis prediction tool, they may be eligible for more aggressive treatment strategies, improving survival and providing maximal palliative effects.

For these reasons, several scoring systems have been developed to predict the survival of patients with BM. Most of these scoring models have been developed by orthopedic surgeons [10,11] or radiation oncologists [12]. Therefore, these scoring models might be influenced by selection biases, as the patients included in their development were only treated with surgical intervention or radiotherapy for bone metastatic lesions. However, the treatment strategy (e.g. chemotherapy, radiation therapy, or surgery) must be decided at the time of the BM diagnosis. Therefore, to determine the individualized optimal strategy, a scoring model based on the clinical factors at the time of the BM diagnosis that affect the cancer-specific survival (CSS) should be used.

We previously developed GU cancer-specific scoring system for predicting the survivals of patients with prostate cancer (PCa), renal cell carcinoma (RCC), or urothelial carcinoma (UC) cancer with BM, called the B-FOM (Bone-Fujimoto-Owari-Miyake) scoring model [1]. The B-FOM score scoring model aids in the selection of the optimal treatment at the BM diagnosis via discussion among urologists, radiation oncologists, oncologists, and orthopedic surgeons. The B-FOM scoring system is a simple survival prediction tool, based on five independent prognostic factors from a multivariable analysis of 180 patients at a single center (i.e. the development cohort). These factors include the type of primary tumor (PCa: 0 points, RCC: 1 point, urothelial [UC]: 3 points), Eastern Cooperative Oncology Group performance status (ECOG-PS) (0–1: 0 points, ≥2: 2 points), the presence of visceral metastasis (absence: 0 points, presence:1 points), Glasgow-prognostic score (GPS) (0:0 points, 1:1 points, 2:2 points), neutrophil-to-lymphocyte ratio (NLR) (normal:0 points, elevated:1 points). To the best of our knowledge, the B-FOM score is the first GU-cancer specific scoring model for predicting the survival of patients with BM. However, the study in which the B-FOM was developed had some limitations, including its single-center nature and the lack of a validation set. Therefore, the objective of this study was to externally validate the B-FOM scoring model using 309 newly diagnosed patients from 10 institutions, and to further refine the B-FOM classification to predict survival with higher accuracy. Moreover, we compared the performance of the resulting modified B-FOM score classification with that of previously reported scoring models.

2. Materials and methods

2.1. Collection of data from patients with bone metastasis

This study was approved by the institutional review board and ethics committee of Nara Medical University (reference no. 1594). Informed consent was obtained via opt-out consent process because of the retrospective nature of this study. The present study used the medical records of patients with GU cancer with BM newly diagnosed at Nara Medical University (original development cohort) and 10 affiliated hospitals (validation cohort) between January 2007 and August 2017. The study protocol is shown in Supplementary figure 1. The B-FOM score was previously developed using a cohort of 180 patients diagnosed and treated at Nara Medical University [1]. In the present study, we used a separate cohort of patients diagnosed and treated at our affiliated hospitals as a validation cohort. Initially, 550 patients were enrolled into the present study; of these, 241 patients were excluded from the analysis because of loss to follow-up, unconfirmed final outcome status, and insufficient clinical data. Thus, the validation cohort finally comprised 309 patients.

We collected the following clinical data needed to calculate the B-FOM score and other representative scoring systems for predicting the survival of patients with BM [10–13]: the types of primary tumor, age, ECOG-PS, presence of visceral metastasis, multiplicity of BM, presence of extraspinal bone metastasis, presence of metastatic fractures and neurological deficit, baseline laboratory data needed to compute the GPS and NLR, previous anticancer systemic therapy, and survival time. GPS was defined as follows: patients with an elevated C-reactive protein (CRP) concentration (>1.0 mg/dL) or hypoalbuminemia (<3.5 g/dL) were classified as having a GPS of 1; those with both abnormalities were classified as having a GPS of 2; and those with neither of these abnormalities were classified as having a GPS of 0. The NLR was calculated by dividing the blood neutrophil count by the blood lymphocyte count. In the present study, we set the cutoff value for an elevated NLR as 3.0 [1]. Survival time was calculated from the diagnosis of BM to the date of death or until the end of the study.

2.2. Genitourinary cancers-specific scoring system for predicting survival in patients with bone metastasis (B-FOM score)

We previously revealed that the types of primary tumors (RCC vs. PCa, UC vs. PCa), ECOG-PS (2 ≤ vs. 0 or 1), the presence of visceral metastases, high GPS (1 vs. 0, 2 vs. 0) and elevated NLR were independent prognostic factors on multivariable analysis in the

Table1

B-FOM score and risk stratification (Takuya O et al. Anticancer Res. 2018; 38: 3097–3103).

Variables	Category	Score
Primary Cancer	Prostate cancer	0
	Renal cell carcinoma	1
	Urothelial carcinoma	3
ECOG-PS	0 or 1	0
	≥2	2
Visceral metastasis	No	0
	Yes	1
GPS	0	0
	1	1
	2	2
NLR	Normal	0
	Elevated	1
Total Score		0–9
Risk classification		
Original classification		
	Low	0
	Intermediate	1,2
	High	3,4
	Very High	≥5
Modified classification		
	Low	0–2
	Intermediate	3,4
	High	≥5

B-FOM score, Bone-Fujimoto-Owari-Miyake score; ECOG-PS, Eastern Cooperative Oncology Group Performance Status; GPS, Glasgow prognostic score; NLR, neutrophil-to-lymphocyte ratio.

This table was cited from Anticancer Res. 2018;38(5):3097-3103 following publisher's approval.

Table 2
Patients characteristics of development cohort and validation cohort.

Variables		Cohorts		p value
		Development cohort	Validation cohort	
Total		180	309	-
Types of primary tumors				0.256†
	Prostate cancer	111 (62%)	209 (68%)	
	Renal cell carcinoma	43 (24%)	55 (18%)	
	Urothelial carcinoma	26 (14%)	45 (14%)	
Age at bone metastasis	Median (IQR)	70 (64–76)	73 (66–79)	0.0084‡
ECOG-PS				0.723†
	0 or 1	132 (73%)	222 (72%)	
	≥2	48 (27%)	87 (28%)	
Visceral metastases				0.012†
	No	119 (66%)	167 (54%)	
	Yes	61 (34%)	142 (46%)	
Multiple bone metastases				0.0273†
	No	31 (17%)	80 (26%)	
	Yes	149 (83%)	229 (74%)	
Extraspinal bone metastases				0.0845†
	No	26 (14%)	64 (21%)	
	Yes	154 (86%)	245 (79%)	
GPS				0.0024†
	0	118 (66%)	178 (57%)	
	1	45 (25%)	64 (21%)	
	2	17 (9%)	67 (22%)	
Baseline Hb (ng/dL)	Median (IQR)	12.8 (11–14)	12.6 (10.9–14)	0.786‡
Baseline PLT (μL)	Median (IQR)	21.05 (16.9–25.8)	22 (17.9–27.9)	0.122‡
Baseline Alb (g/dL)	Median (IQR)	4.2 (3.8–4.4)	3.9 (3.4–4.3)	< 0.001‡
Baseline CRP (mg/dL)	Median (IQR)	0.2 (0.1–1.83)	0.5 (0.1–2.5)	0.121‡
Baseline ALP (U/L)	Median (IQR)	328 (241–512)	379.5 (248–765)	0.0216‡
Baseline NLR	Median (IQR)	2.925 (1.99–3.82)	2.857 (2.0–4.43)	0.350‡
NLR	Normal	92 (51%)	159 (51%)	0.941†
	Elevated	88 (49%)	150 (49%)	
Anti-cancer systemic therapy				<0.001†
	No	120 (67%)	258 (84%)	
	Yes	60 (33%)	51 (16%)	
Radiotherapy for bone metastases				0.0228†
	No	123 (68%)	240 (78%)	
	Yes	57 (32%)	69 (22%)	
Surgery for bone metastases				0.005†
	No	159 (88%)	294 (95%)	
	Yes	21 (12%)	15 (5%)	
Follow-up period (months)	Median (IQR)	25 (10–47.25)	17 (6–36)	0.001‡

ECOG-PS, Eastern Cooperative Oncology Group Performance Status; GPS, Glasgow prognostic score; Hb, hemoglobin; CRP, C-reactive protein; ALP, alkaline phosphatase; NLR, neutrophil-to-lymphocyte ratio; IQR, interquartile range.
†: Chi-square test.
‡: Man-Whitney *U* test.

development cohort [1]. The B-FOM scoring system was developed by scoring each risk factor according to the regression coefficients in the multivariable analysis. The B-FOM score for each patient was calculated as the sum of five scores representing significant prognostic factors and ranged from 0 to 9. We originally classified patients into the following 4 risk groups according to the B-FOM score: low (0 points), intermediate (1 or 2 points), high (3 or 4 points), and very high (≥5 points). However, in this risk classification, the low-risk group included only patients with PCa, limiting its usefulness to clinicians. Thus, in the present study, we used a modified B-FOM risk classification to improve the performance and make it more useful to clinicians (Table 1) and evaluated the performance of both the original and modified classifications. For the modified classification according to B-FOM risk, patients were stratified into 3 risk groups including low (0–2 points), intermediate (3, 4 points), and high (≥5 points).

2.3. Statistical analysis

A descriptive analysis was performed to compare the demographic and clinical features between development and validation cohorts (Table 2). Baseline characteristics in each cohort were compared using the Mann–Whitney *U* test or Chi-square test. CSS curves of different classifications were evaluated by the Kaplan-Meier method and compared by using the log-rank test. Receiver operating characteristic (ROC) curves and the area under the curve (AUC) were calculated to evaluate the performance of the B-FOM score and other scoring systems for predicting the outcome mortality at 6, 12, and 24 months. A *p*-value < 0.05 was considered statistically significant. The Kaplan–Meier method and log-rank test were performed using GraphPad Prism 7.00 (GraphPad Software, San Diego, CA, USA). The ROC curves and AUC were calculated using SPSS for Windows (version 20.0; IBM Corp., Armonk, NY, USA).

3. Results

3.1. Patient characteristics

The baseline characteristics of the 180 patients in the original development cohort (1) and the 309 patients in the validation cohort are described in Table 2. The median follow-up times were 25 (interquartile range, IQR: 10–47.25) and 17 (IQR: 6–36) months
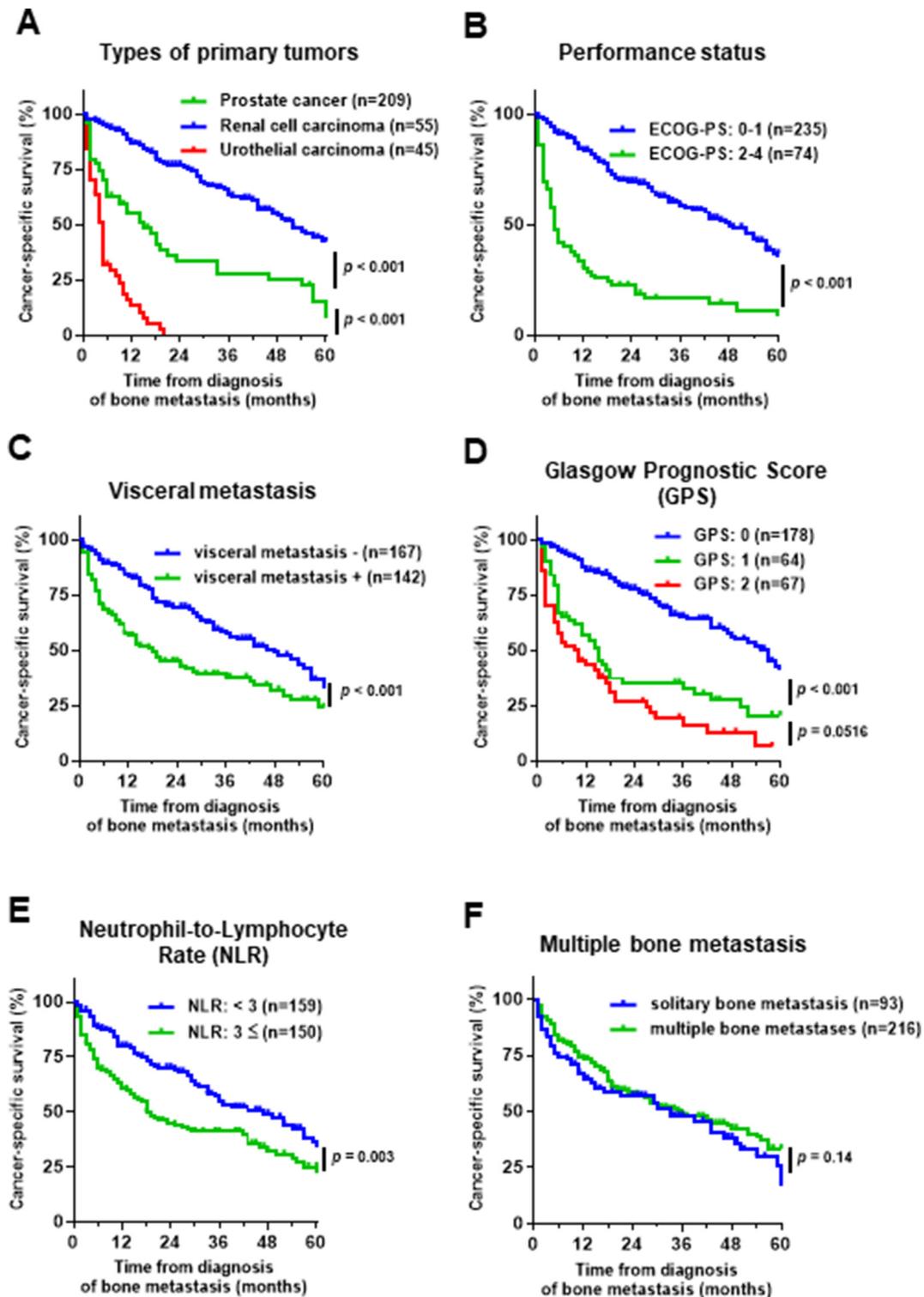
Fig. 1. Kaplan-Meier curves of candidate predictors for the cancer-specific survival of patients with genitourinary cancer with bone metastases in an external validation cohort. The type of primary tumor (RCC *vs.* PCa, UC *vs* PCa), ECOG-PS ($\geq$2 *vs* 0 or 1), presence of visceral metastases, high GPS (1 *vs.* 0, 2 *vs.* 0), and elevated NLR (NLR: $\geq$3) were significantly associated with poor survival. PCa, prostate cancer; RCC, renal cell carcinoma; UC, urothelial carcinoma; ECOG-PS, Eastern Cooperative Oncology Group performance status; GPS, Glasgow-prognostic score; NLR, neutrophil-to-lymphocyte ratio.

in development and validation cohorts, respectively. There were no significant differences in the distribution of primary cancers and ECOG-PS between development and validation cohorts. The proportion of patients with visceral metastasis was significantly higher in the validation cohort than in the development cohort (p = 0.012). Regarding laboratory data, the proportion of patients

with GPS 2 was significantly higher in the validation cohort than in the development cohort; however, there was no significant difference in NLR between the two cohorts. Significantly more patients received aggressive treatment including systemic chemotherapy (33 *vs.* 16%, p < 0.001), radiation therapy (32 *vs.* 22%, p = 0.028), and surgical intervention or bone metastatic

Table 3

Analyses of clinical variables predicting cancer-specific survival in validation cohort.

Variables	Cancer-specific survival					
	Univariable†			Multivariable †		
	HR	95% CI	P value	HR	95% CI	P value
Primary Cancer						
Prostate cancer	1					
Renal cell carcinoma	2.86	1.96–4.18	<0.001	2.6	1.77–3.80	<0.001
Urothelial carcinoma	11.6	7.57–17.8	<0.001	7.09	4.52–11.14	<0.001
ECOG-PS						
0 or 1	1			1		
≥2	4.1	3.0–5.65	<0.001	2.54	1.79–3.63	<0.001
Multiple bone metastases						
Solitary	1					
Multiplicity	0.78	0.57–1.09	0.15			
Visceral metastases						
No	1			1		
Yes	1.86	1.37–2.53	<0.001	1.1	0.77–1.55	0.62
GPS						
0	1			1		
1	2.67	1.82–3.90	<0.001	1.79	1.19–2.69	0.006
2	4.51	3.11–6.54	<0.001	2.32	1.50–3.59	<0.001
NLR						
Normal (<3)	1			1		
Elevated (≥3)	1.8	1.32–2.46	<0.001	1.2	0.86–1.70	0.27

† COX regression hazard analysis.

lesions (12 *vs.* 5%, $p = 0.005$) in the development cohort than in the validation cohort.

3.2. Externally validated predictive factors of the B-FOM score associated with cancer-specific survival

The Kaplan-Meier curves demonstrated that the survival of patients with RCC ($p < 0.001$) and UC ($p < 0.001$) was significantly shorter than that for patients with PCa (Fig. 1A). Moreover, poor PS ($p < 0.001$) (Fig. 1B), the presence of visceral metastasis ($p < 0.001$) (Fig. 1C), high GPS (1 *vs.* 0, 2 *vs.* 0) ($p < 0.001$) (Fig. 1D), and elevated NLR ($p = 0.003$) (Fig. 1E) were significantly associated with a lower survival rate. In contrast, the presence of multiple BMs, which is a prognostic predictive factor in other scoring systems including the revised Tokuhashi score [10], Tomita score [11], van der Linden score [12], and modified Baur score [13], was not associated with shorter survival (Fig. 1F). The result of univariable and multivariable analysis was described in Table 3. On univariable analysis, the type of primary tumors (RCC *vs.* PCa, UC *vs.* PCa), poor ECOG-PS, presence of visceral metastases, high GPS (1 *vs.* 0, 2 *vs.* 0) and elevated NLR were found to be significantly associated. In contrast, the presence of multiple BMs was not significantly associated with CSS ($p = 0.15$). On multivariable analysis, the type of primary tumor, ECOG-PS, and high GPS were identified as independent predictive factors (Table 3).

3.3. Comparative analysis of the performance of the B-FOM scoring model with other scoring models

The Kaplan-Meier curves for CSS based on the original and modified risk classifications according to the B-FOM scoring model and other representative scoring systems (i.e. the revised Tokuhashi score [10], Tomita score [11], van der Linden score [12], and modified Baur score [13]) are shown in Figs. 2 and 3. In the validation cohort, there was no significant difference in survival between the low- and intermediate-risk groups using the original B-FOM classification (Fig. 2B). However, survival curves according to the modified B-FOM classification successfully stratified the patients according to the risk in the development and validation cohorts (Fig. 2C and D). Therefore, the modified classification according

to the B-FOM score is more relevant to the CSS of patients with GU cancer with BM than the original classification.

Next, we compared the performance of the modified B-FOM classification with other scoring models using data from the validation cohort (Fig. 4 and Table S1). Risk classification according to the revised Tokuhashi score and modified Baur score failed to show a significant difference in survival between low- and intermediate-risk groups ($p = 0.83$ and $p = 0.264$, respectively) (Fig. 3A and D). Moreover, with risk classification according to Tomita score, the CSS was shorter in the intermediate-risk group (Median CSS: 19 months) than in the high-risk group (Median CSS: 43 months) (Fig. 3B and Table S1). In addition, the low-risk group according to van der Linden score classification only comprised patients with breast cancer, thus, this scoring model is not useful for predicting survival in GU cancer (Fig. 3C).

On COX regression analysis, using the modified B-FOM risk classification, the hazard ratio (HR), with the low-risk group as the reference, was 1.998 (95% confidence interval; CI: 1.29–3.09, $p = 0.002$) and 12.117 (95% CI: 8.31–17.84, $p < 0.001$) for the intermediate- and high-risk groups, respectively. In contrast, using the risk classification according to the revised Tokuhashi, Tomita, and modified Baur scoring models, the HRs for intermediate-risk group (relative to the low-risk group) were 1.019 ($p = 0.936$), 1.793 ($p = 0.05$), and 1.379 ($p = 0.059$), respectively (Table S1). Based on these findings, the modified risk classification according to the B-FOM score was the most accurate tool for predicting CSS in patients with GU cancer with BM among these scoring models.

4. Comparative analysis of the accuracy of predicting short-term mortality using the B-FOM and other scoring models

The area under the ROC curves (AUC) for predicting mortality using the B-FOM and other scoring models are shown in Fig. 4 and Table S2. The AUCs of the modified classification according to the B-FOM score for predicting mortality at 6 months, 1 year, and 2 years reached 0.895 (95% CI: 0.849–0.945), 0.856 (95% CI: 0.801–0.911), and 0.815 (95% CI: 0.761–0.868), respectively. These results were significantly higher than those obtained using other scoring models (Table S2). In addition, using development cohort for a resampling method as a validation sample to evaluate the
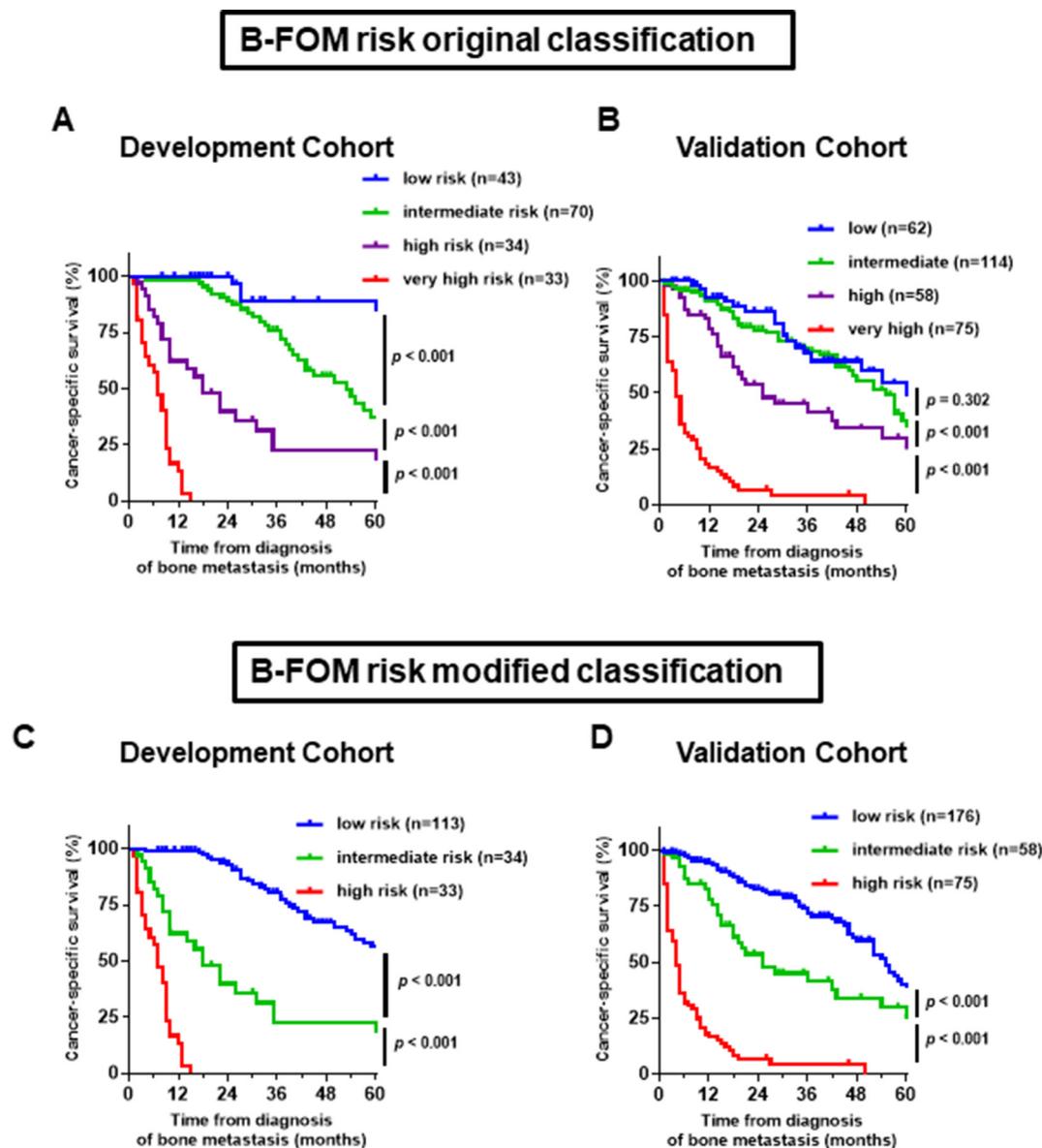
Fig. 2. Kaplan–Meier curves of the original and revised risk groups based on the Bone-Fujimoto-Owari-Miyake (B-FOM) score in the development and validation cohorts. In the validation cohort, there was no significant difference in survival rate between low- and intermediate-risk groups by the original risk classification. However, the survival curves of the modified risk classification according to the B-FOM score successfully stratified the patients in the development and validation cohorts. Fig. 2A was taken from Anticancer Research, 2018;38(5):3097-3103 following the publisher's approval.

performance of the modified classification according to B-FOM score, the AUCs of the modified classification for predicting shorter mortality at 6 months,1 year, and 2 years reached 0.860 (95% CI: 0.785–0.934), 0.928 (95% CI: 0.885–0.971), and 0.907 (95% CI: 0.854–0.960), respectively (Supplementary figure 2). Therefore, the modified classification based on B-FOM score predicts short-term mortality with higher accuracy than do other scoring systems.

5. Discussion

To the best of our knowledge, B-FOM score is the first GU-cancer-specific scoring model for predicting the survival of patients with BM. An accurate prognosis prediction is vitally important to determine the optimal individualized strategy. Those with longer expected survival at the diagnosis of BM could be eligible candidates for more aggressive interventions, including

radiotherapy and surgical interventions for local lesions, to control local tumor progression and prolong survival. In contrast, if a patient is expected to have shorter survival, palliative treatments to improve individual pain or neurological compromise could be considered. In this multi-institutional study, we externally validated the performance of this scoring model for predicting individual CSS in the diagnosis of BM. In addition, we compared the prediction accuracy of this scoring model with that of other representative scoring systems predicting the survival of patients with BM, including the revised Tokuhashi score [10], Tomita score [11], van der Linden score [12], and modified Baur score [13].

We previously developed a B-FOM score based on 5 independent predictors of CSS by multivariable analysis including the types of primary tumor (RCC *vs.* PCa, UC *vs.* PCa), ECOG-PS ($2 \leq$ *vs.* 0 or 1), presence of visceral metastases, high GPS (1 *vs.* 0, 2 *vs.* 0), and elevated NLR [1]. In the present study, the Kaplan-Meier survival curve using the validation cohort demonstrated that the candidate
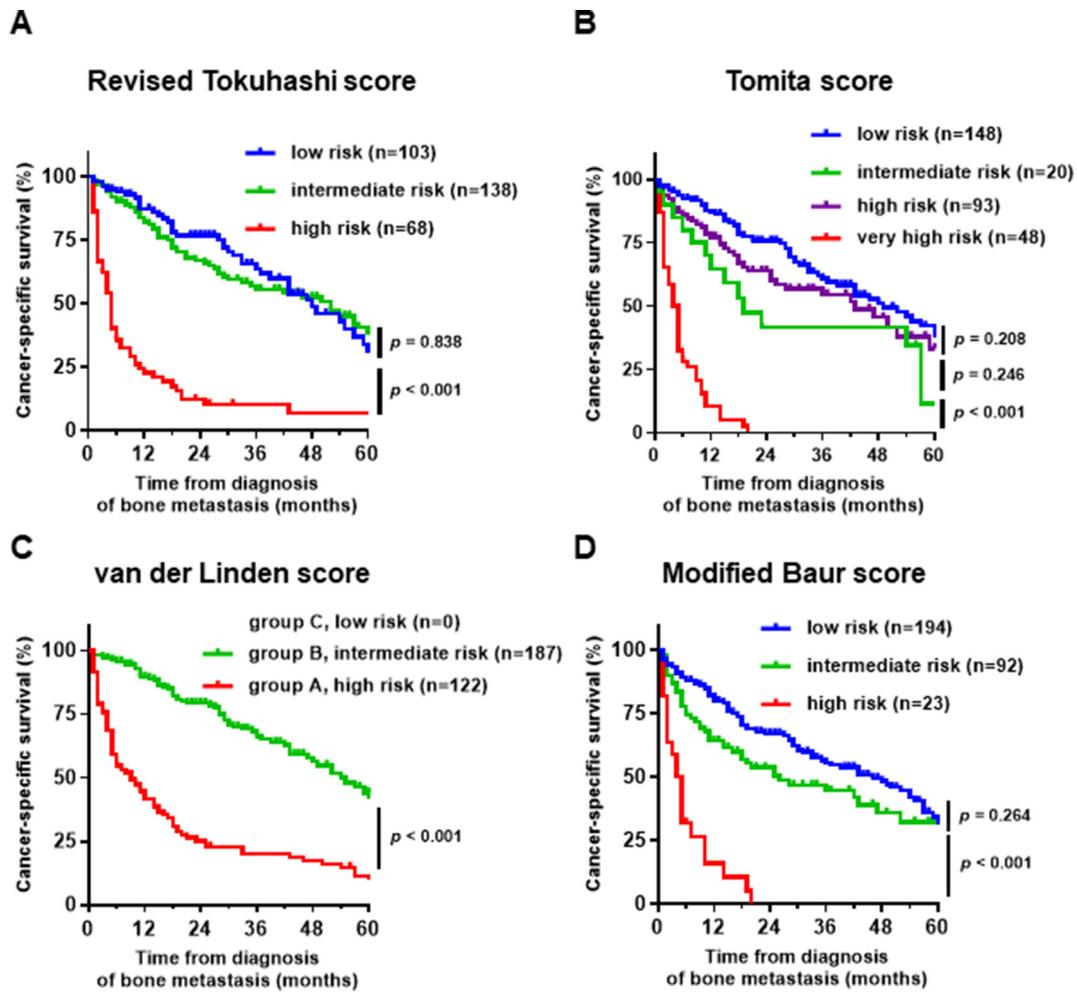
Fig. 3. Kaplan–Meier curves of risk groups based on four representative risk scores, including the revised Tokuhashi score (A) (10), Tomita score (B) (11), van der Linden score (C) (12), and modified Baur score (D) (13), did not show good discrimination among prognostic groups in the validation cohort.
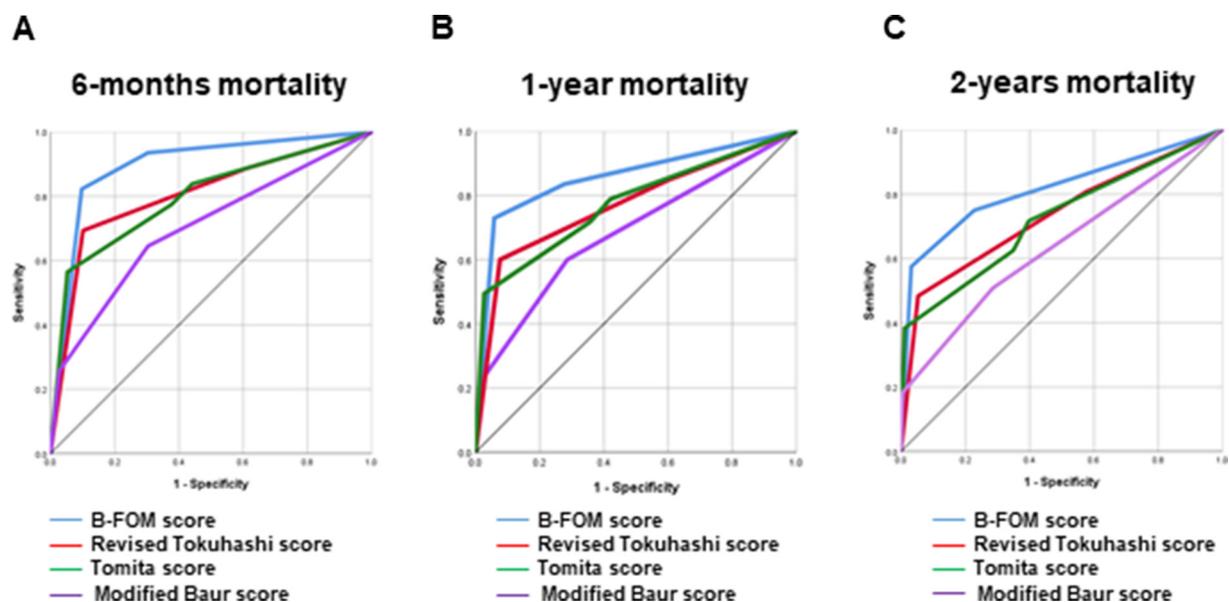
Fig. 4. Prognostic performance of the B-FOM score as assessed by receiver operating characteristic (ROC) curves and the area under the curve (AUC). The accuracy of predicting the mortality at 6, 12, and 24 months was higher with the modified risk classification according to the B-FOM score than with other scoring models.

predictors were significantly associated with poor survival. Moreover, the types of primary tumor, ECOG-PS, and high GPS independently predicted CSS on multivariable analysis. The weighting score for each type of primary tumor is extremely important for constructing this scoring model, as with other scoring models, considering the nature of each GU cancer. Among GU cancers, UC was assigned the highest score because the survival of patients with metastatic UC was extremely short (median CSS: 5 months *vs.* 15 months (RCC), 52 months (PCa)). Although the latest monoclonal antibodies against programmed death 1 (PD-1) have shown strong antitumor activity in many types of tumors, a large randomized trial demonstrated that the overall survival of patients with UC treated with pembrolizumab was 10.3 months (*vs.* 7.4 months in the chemotherapy group) [14].

Visceral metastasis has been demonstrated as a strong predictor, especially in advanced PCa (15, 16). Because the presence of visceral metastasis could be an indicator of systemic disease, it is included as a prognostic factor in most scoring models [10–12,15,16], as well as the B-FOM score. In contrast, the presence of multiple BMs, which was included in the revised Tokuhashi score, Tomita score, and modified Baur score, were not associated with poor survival by the Kaplan-Meier survival curve and univariable analysis in both the development [1] and validation cohorts. This result was likely due to the nature of GU cancers. Patients were more likely to have multiple BMs in PCa (78%) than in RCC (43%) and UC (63%) (data not shown). Even if a patient had multiple BMs, the survival of patients with advanced PCa was longer; the median survival of patients with metastatic PCa in the present study was 52 months, and two previous large trials demonstrated that the median survival of patients with advanced PCa was 43–45 and 46–48 months [17,18]. Therefore, a GU-cancer-specific scoring model should not include multiple BMs as a predictive factor. Another peculiarity of the B-FOM scoring model is the inclusion of laboratory data at the time of BM diagnosis. In particular, high GPS was strongly associated with poor survival in the present study (1 *vs.* 0; HR 1.79, 95% CI 1.19–2.69, p = 0.006, 2 *vs.* 0; HR 2.32, 95% CI 1.50–3.59, p < 0.001). GPS, a combination of CRP and albumin levels, reflects systemic inflammation and nutritional status. Recently, several studies demonstrated that high GPS was a strong prognostic factor for PCa, RCC, and UC [19–21]. On the other hand, elevated NLR was not identified as an independent prognostic factor on multivariable analysis using the validation cohort, but the Kaplan-Meier survival curve showed that elevated NLR was associated with poor survival (p = 0.003). Elevated NLR has been demonstrated as a prognostic factor in patients with GU cancer [22–24]. Although we set the cutoff level of NLR at 3.0 in this scoring model, this might need adjustment, as different levels were set in previous studies [22–24].

The revised Tokuhashi score is one of the most popular scoring systems for spinal metastases [10]. This scoring system was developed using patients with spinal metastasis treated by orthopedic surgeons, who reported that if the predicted survival time is more than 12 months based on this scoring model, more aggressive excisional surgery can be selected; however, if the life expectancy is ≤ 6 months, conservative treatment or palliative surgery is the optimal therapeutic modality. In contrast, van der Linden et al. [12] analyzed patients without neurological symptoms who received radiotherapy and Rades et al. [25] analyzed patients who received radiotherapy for metastatic spinal cord compression. These authors did not investigate clinical data at the time of BM diagnosis, and selection biases could have been present during model development. We evaluated the clinical data at the time of BM diagnosis and developed a GU-cancer-specific scoring model, with the consideration of the nature of GU cancer with BM. In addition, we previously classified 4 risk groups according to the B-FOM scoring model [1]. In the present study, we modified

the risk classification because the low-risk group based on the original classification only included patients with PCa and there was no significant difference in CSS between the low- and intermediate-risk group in the validation cohort (Fig. 2B). Using the modified risk classification, patients in each group were successfully stratified in both the development and validation cohorts (Fig. 2C, D). In contrast, the Kaplan-Meier survival curves did not show good discrimination among prognostic groups using other scoring models using other scoring models (Fig. 3). Moreover, the accuracy of predicting mortality at 6, 12, or 24 months was significantly higher with the modified risk classification according to the B-FOM score than with other scoring models. Based on these findings, the B-FOM scoring model is an easy to use and novel prognostic tool for GU cancers with BM, with higher accuracy than other tools.

The present study has some limitations. First, it was a retrospective study. Second, the treatment for BMs was not consistent and was at the discretion of each attending physician. In addition, there were relatively small numbers of patients who underwent surgery (5%) or radiotherapy (22%) in the validation cohort. Therefore, it is difficult to draw a strict conclusion regarding treatment strategy.

6. Conclusion

The B-FOM scoring model is the first GU-cancer-specific scoring system for predicting the survival of patients with BM. This study demonstrated that the B-FOM score predicts survival in GU cancers with BM with higher accuracy than that of other previously reported scoring models. Clinical physicians including not only urologists but also orthopedic surgeons and radiation oncologists can better select the optimal individualized strategies at the time of BM diagnosis using the B-FOM scoring model.

7. Funding support

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.

Acknowledgments

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jbo.2020.100344.

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