Prognostic assessment of patients with bone metastatic renal cell cancer treated with palliative radiotherapy

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Abstract. The present study investigated the prognosis of patients who received palliative radiotherapy (RT) for bone metastases (BMs) from renal cell cancer (RCC), and assessed the prognostic factors specific to BMs from RCC. A total of 109 patients with RCC and BMs who underwent RT for the first time were included in the study. Prognostic factors were evaluated using multivariate analysis and a scoring system based on regression coefficients was devised. The median follow-up time was 9 months, and the 0.5-year overall survival (OS) rate was 73.0%. In the multivariate analysis, the significant prognostic factors were higher performance status (≥2), no control of the primary site, disseminated metastasis, lymph node metastasis and multiple BMs. A score of 1 point was assigned to each risk factor. The median OS times were 19.0 and 5.0 months in patients with a total score of ≤1 (n=49) and >1 (n=60), respectively (P<0.01). In conclusion, a comprehensive prognostic assessment using these factors may be useful for predicting the prognoses of patients with BMs from RCC. In addition, this scoring system may be useful in selecting the optimal RT dose.

Introduction

Distant metastases commonly occur in the bone (1). Bone metastases (BMs) occur in approximately 30% of metastatic renal cell cancers (RCC), and most patients with BMs do not expect a good prognosis (1-year OS, approximately 30%) (2,3).

Hypofractionated RT (e.g., a single fraction of 8 Gy) is as effective as fractionated RT for pain relief and metastatic spinal cord compression (MSCC) in the BMs from RCC (4). However, the radiographic local control of BMs receiving RT is insufficient with hypofractionated RT, and the re-RT rate is higher for hypofractionated RT than for fractionated RT (4-9). Therefore, hypofractionated RT may be unsuitable for patients with an expected long-term prognosis, and the prediction of life expectancy is crucial at the time of RT for BMs from RCC.

Several scoring systems have been developed for patients with bone metastasis (10-13). In one of these scoring systems, Katagiri *et al* devised a very precise prognostic scoring system for patients with BMs from various primary cancers (10). However, the recent remarkable progress in systemic therapy, tyrosine kinase inhibitors (TKI), and immune checkpoint inhibitors (ICI) has improved the prognosis of patients with advanced RCC (14-18). Although several disease-specific prognostic scoring systems for BMs have been devised. In addition, the International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) scoring system (19,20) and the Memorial Sloan-Kettering Cancer Center (MSKCC) prognostic scoring systems (21) are well-known prognostic scoring systems for metastatic RCC. However, few prognostic scoring systems are useful for the radiation oncologists when selecting the RT dose for BMs from RCC (22-25). Therefore, to select the optimal RT dose for BMs from RCC, we assessed the prognostic factors in RCC patients with BMs and devised a prognostic scoring system.

Materials and methods

Study population. Between January 2010 and March 2023, 109 consecutive RCC patients were treated with initial RT for BMs at our institutions (Ehime University Hospital, Toon, Japan, n=50; Ehime Prefectural Central Hospital, Matsuyama, Japan, n=38; National Hospital Organization Shikoku Cancer Center, Matsuyama, Japan, n=21). RCC patients with BMs were referred by an attending physician to a radiation oncologist for palliative RT for the following reasons: i) Pain relief with or without prevention of pathological fractures, and ii) metastatic spinal cord compression (MSCC) with or without pain and/or

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neurological symptoms. The Ethics Committee of National Hospital Organization Shikoku Cancer Center approved this retrospective study (registration no. 2023-525).

BMs was detected using computed tomography (CT, n=109), bone scintigraphy (n=22), 18F fluorodeoxyglucose positron-emission tomography and CT (n=31), or magnetic resonance (MR, n=28) scans. Performance status (PS) was evaluated using the Eastern Cooperative Oncology Group scale.

Radiotherapy. The patients received three-dimensional conformal RT delivered using 4-10 MV photons with a linear accelerator (Clinac 21EX, Clinac iX, or TrueBeam, Varian Medical Systems).

The most common RT dose was 30 Gy in 10 fractions (n=39, 34.9%). The other fraction schedules were as follows: 1x8 Gy (n=8), 5x4 Gy (n=4), 4x5 Gy (n=1), 13-15x3 Gy (n=32), 15-20x2.5 Gy (n=9), 20-25x2 Gy (n=5), and 5x4 Gy + 8x2 Gy (n=1).

Statistical analyses. The survival rate was calculated using the Kaplan-Meier method with log-rank test. The Cox proportional hazard model was used for univariate and multivariate analyses to determine the hazard ratios (HRs), including 95% confidence intervals (CIs) and P-values. Factors such as age, sex, PS, histologic type, control of the primary tumor of the kidney (primary site), brain metastasis, liver metastasis, lung metastasis, disseminated metastasis, lymph node metastasis, number of bone metastatic lesions, bone metastatic site, RT site, pathological fracture, neurological symptoms, use of bone-modifying agents (BMAs), pre-RT targeted therapies (TTs), and pre-RT laboratory data were analyzed using univariate analysis. Because the important factors were not clear in the previous studies, factors with P<0.10 on univariate analysis were subjected to multivariate analysis. In multivariate analysis and log-rank tests, P<0.05 was considered to indicate a statistically significant difference and a scoring system based on regression coefficients in the multivariate analysis was devised. Statistical analyses were performed using JMP software (JMP version 14.3.0; SAS Institute, Cary, North Carolina, United States).

Results

Clinical characteristics. The patient characteristics are listed in Table I. A total of 41 (37.6%), 22 (20.2%), and 46 (42.2%) patients had single, 2-3, and >3 BMs, respectively. A total of 54 (50.5%) patients underwent pre-RT TTs such as sorafenib, sunitinib, axitinib, pazopanib, everolimus, temsirolimus, cabozantinib, nivolumab, and ipilimumab.

Pre-RT laboratory data were collected using the Katagiri scoring system (10). Only eight patients showed critically abnormal laboratory data (platelets, 3; serum calcium, 5; total bilirubin, 0). Therefore, abnormal [CRP ≥0.4 mg/dl, lactate dehydrogenase (LDH) ≥250 IU/l, or serum albumin <3.7 g/dl] and critically abnormal (platelet <100,000/l, serum calcium ≥10.3 mg/dl, or total bilirubin ≥1.4 mg/dl) laboratory data were included within the same group as abnormal laboratory data.

Among the 109 patients, 62 (56.9%) died and 47 (43.1%) survived at the latest follow-up. The median follow-up time of OS was 9.0 months (range, 0.5-146.0 months), and the 0.5- and 1-year OS rates were 73.0 and 59.4%, respectively (Fig. 1). In addition, the median follow-up time for the survival of living and dead patients at the final follow-up was 10.0 months (range, 1.0-146.0 months) and 9.0 months (range, 0.5-98.0 months), respectively.

Prognostic factors for patients with BMs from RCC. Because de novo, which means 'RCC patients with BMs at the time of initial diagnosis, and the primary site control cases did not differ significantly in OS (HR, 1.40; 95% CI, 0.70-2.80; P=0.33), the control evaluation of the primary site was classified into two groups (control or de novo vs. no control).

In the univariate analysis, PS (<2 vs. ≥2; HR, 2.16; 95% CI, 1.30-3.61; P<0.01), primary site (control or de novo vs. no control; HR, 2.67; 95% CI, 1.30-5.47; P=0.01), lung metastasis (no vs. yes; HR, 1.68; 95% CI, 0.99-2.86; P=0.05), disseminated metastasis (no vs. yes; HR, 3.00; 95% CI, 1.54-5.88; P<0.01), lymph node metastasis (no vs. yes; HR, 2.23; 95% CI, 1.31-3.80; P<0.01), number of bone metastasis (single vs. multiple; HR, 2.31; 95% CI, 1.29-4.14; P<0.01), and pre-RT laboratory data (normal vs. abnormal; HR, 2.40; 95% CI, 1.13-5.12; P=0.02) were significantly associated with OS (Table II).

In the multivariate analysis, ECOG-PS (<2 vs. ≥2; HR, 1.84; 95% CI, 1.06-3.18; P=0.03), primary site (control or de novo vs. no control; HR, 3.24; 95% CI, 1.51-6.95; P<0.01), disseminated metastasis (no vs. yes; HR, 2.36; 95% CI, 1.12-4.97; P=0.02), lymph node metastasis (no vs. yes; HR, 1.91; 95% CI, 1.04-3.51; P=0.04), and the number of bone metastasis (single vs. multiple; HR, 2.56; 95% CI, 1.38-4.75; P<0.01) were significantly associated with reduced OS (Table II).

RT course length [long (>10 fractions) vs. short (≤10 fractions); HR, 1.78; 95% CI, 1.08-2.94; P=0.02] was significantly associated with OS in the univariate analysis, but this factor was not included in the multivariate analysis because of selection bias.

Prognosis according to the devised prognostic scoring system. A prognostic scoring system using the regression coefficients of significant prognostic factors in multivariate analysis was developed (Tables II and III). ECOG-PS, primary sites, disseminated metastasis, lymph node metastasis, and number of bone metastatic lesions were used to create a scoring system for the estimation of survival. Because all regression coefficients were between 0.3 and 0.6, one point was assigned to each factor. The associations between the total points and the 0.5- and 1-year OS rates are listed in Table IV, and the corresponding Kaplan-Meier curves are shown in Fig. 2.

We classified patients with BMs from LC into two groups and stratified them according to our scoring system. The median OS was 19.0 months for the favorable group (total point score 0-1) (n=49) and 5.0 months for the unfavorable group (total point score 2-4) (n=60) (p<0.01, log-rank test). The OS curves are shown in Fig. 3.

Discussion

This is the first study to identify the factors that help radiation oncologists' selection the optimal RT dose for BMs from RCC. Based on our multivariate analysis, a higher ECOG-PS

Table I. Patient characteristics.

Characteristic	Value
Median age, years (range)	69 (42-89)
Age, n (%)	
<70 years	59 (54.1)
≥70 years	50 (45.9)
Sex, n (%)	
Male	84 (77.1)
Female	25 (22.9)
ECOG-PS, n (%)	
<2	54 (49.5)
2	29 (26.6)
>2	26 (23.9)
Histologic type, n (%)	
Clear cell	101 (92.7)
Clear cell with spindle cell	5 (4.6)
Papillary	2 (1.8)
Collecting duct	1 (1.0)
Primary site, n (%)	
Control of primary site	72 (66.0)
Surgery	65 (59.6)
ATs	7 (6.4)
No control of primary site	10 (9.2)
Surgery	4 (3.7)
ATs	6 (5.5)
De novo	27 (24.8)
Brain metastasis, n (%)	
Yes	10 (9.2)
No	99 (90.8)
Liver metastasis, n (%)	
Yes	17 (15.6)
No	92 (84.4)
Lung metastasis, n (%)	
Yes	66 (60.6)
No	43 (39.4)
Lymph metastasis, n (%)	
Yes	35 (32.1)
No	74 (67.9)
Disseminated metastasis, n (%)	
Yes	12 (11.0)
No	97 (89.0)
Number of bone metastatic lesions, n (%)	
1	41 (37.6)
2-3	22 (20.2)
>3	46 (42.2)
Bone metastatic site, n (%)	
Only vertebral	32 (29.4)
Only non-vertebral	33 (30.3)
Others	44 (40.4)
Pathological fracture, n (%)	
Yes	15 (13.8)
No	94 (86.2)
RT dose (BED10), n (%)	
<39.0 Gy	12 (11.0)
39.0 Gy (=3 Gy x 10 fraction)	36 (33.0)
>39.0 Gy	61 (56.0)
RT sites, n (%)	
Vertebral	65 (59.6)
Others	44 (40.4)
BMAs, n (%)	
Yes	60 (55.0)
No	49 (45.0)
Pre-RT TTs, n (%)	
Yes	54 (50.5)
No	55 (49.5)
Pre-RT laboratory data	
Median CRP, mg/dl (range)	0.98 (0.02-23.33)
Median LDH, U/l (range)	197 (116-1,017)
Median albumin, g/dl (range)	3.6 (1.8-4.6)
Median platelet, x$10^4/\mu$l (range)	25.2 (3.4-63)
Median Ca, mg/dl (range)	9.1 (7.6-11.3)
Median T-Bil, mg/dl (range)	0.5 (0.2-1.2)

ECOG PS, Eastern Cooperative Oncology Group Performance Status; ATs, antineoplastic therapies; TTs, targeted therapies; RT, radiotherapy; BED, biologically effective dose; BMAs, bone modifying agents; CRP, C-reactive protein; LDH, lactate dehydrogenase; Ca, calcium; T-Bil, total bilirubin.

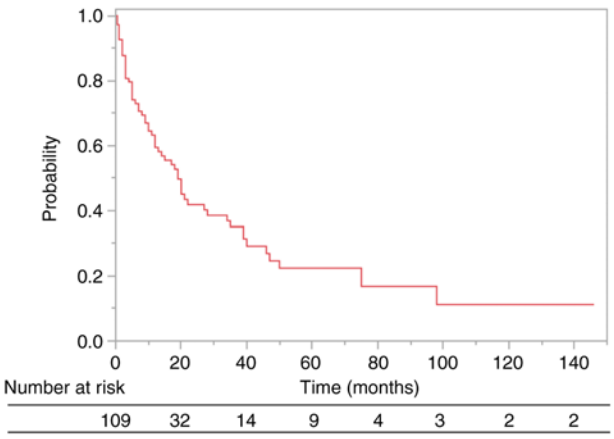

Figure 1. Kaplan-Meier curves of overall survival rate in renal cell carcinoma patients with bone metastases.

score, no control of the primary sites, disseminated metastasis, lymph node metastasis, and multiple bone metastases were important unfavorable prognostic factors for survival. Based on the number of risk factors, patients with BMs from RCC were classified into two groups [median OS: favorable (0-1 point), 19.0 months; unfavorable (2-4 points), 5.0 months].

Table II. Survival rates after RT and results of univariate and multivariate analyses.

Characteristic	1-year survival, %	Univariate analysis		Multivariate analysis		Regression coefficient
		HR (95% CI)	P-value	HR (95% CI)	P-value	
Age, <70 years vs. ≥70 years	61.0 vs. 57.2	1.39 (0.83-2.33)	0.21	-	-	-
Sex, male vs. female	64.2 vs. 47.3	1.53 (0.87-2.69)	0.14	-	-	-
ECOG-PS, 0-1 vs. 2-4	78.0 vs. 41.1	2.16 (1.30-3.61)	<0.01	1.84 (1.06-3.18)	0.03	0.31
Histologic type, clear cell vs. others	61.8 vs. 37.5	1.51 (0.65-3.53)	0.34	-	-	-
Primary site, control or de novo vs. no control	64.1 vs. 20.0	2.67 (1.30-5.47)	0.01	3.24 (1.51-6.95)	<0.01	0.59
Brain metastasis, no vs. yes	59.5 vs. 58.3	1.17 (0.53-2.59)	0.70	-	-	-
Liver metastasis, no vs. yes	62.5 vs. 44.8	1.43 (0.76-2.70)	0.27	-	-	-
Lung metastasis, no vs. yes	62.9 vs. 57.1	1.68 (0.99-2.86)	0.05	1.31 (0.74-2.30)	0.36	0.13
Disseminated metastasis, no vs. yes	63.4 vs. 30.0	3.00 (1.54-5.88)	<0.01	2.36 (1.12-4.97)	0.02	0.43
Lymph node metastasis, no vs. yes	64.7 vs. 48.7	2.23 (1.31-3.80)	<0.01	1.91 (1.04-3.51)	0.04	0.32
Number of bone metastatic lesions, single vs. multiple	73.4 vs. 51.8	2.31 (1.29-4.14)	<0.01	2.56 (1.38-4.75)	<0.01	0.47
Bone metastatic site, only spine vs. others	57.2 vs. 60.3	1.33 (0.73-2.42)	0.35	-	-	-
RT sites, only spine vs. others	57.4 vs. 62.8	1.19 (0.71-2.01)	0.50	-	-	-
Pathological fracture, no vs. yes	58.7 vs. 64.3	1.03 (0.53-1.99)	0.93	-	-	-
Neurological symptom, no vs. yes	61.4 vs. 58.3	1.22 (0.71-2.08)	0.47	-	-	-
Use of BMAs, no vs. yes	51.4 vs. 63.3	0.71 (0.43-1.17)	0.17	-	-	-
Pre-RT TTs, no vs. yes	63.8 vs. 56.3	1.30 (0.78-2.16)	0.31	-	-	-
Pre-RT laboratory data, normal vs. abnormal	79.4 vs. 55.3	2.40 (1.13-5.12)	0.02	1.83 (0.82-4.10)	0.14	0.30

ECOG PS, Eastern Cooperative Oncology Group Performance Status; RT, radiotherapy; BMAs, bone modifying agents; TTs, targeted therapies.

Katagiri *et al* proposed a scoring system for predicting patients with BMs (10). Although this scoring system is one of the most precise scoring systems, previous study suggested that its prognostic factors may be influenced by the high frequency of bone metastases from breast and prostate cancer (23). Therefore, predicting the prognosis of patients with BMs from RCC alone is important for selecting the optimal palliative RT dose. In this study, internal metastases (brain, liver, and lung metastases) were not a prognostic factor in patients with BM from RCC, in contrast to the Katagiri scoring system. In addition, lack of control of primary sites and lymph node metastasis were new prognostic factors for patients with BM from RCC, which were not included in the Katagiri scoring system. Fan *et al* also suggested that these are important prognostic factors for patients with BMs from RCC (24). These factors should be included as prognostic and predictive factors when selecting the optimal RT dose for BMs from RCC. In addition, similar to the study by Fan *et al* (24), pre-RT TTs did not appear to influence the prognosis of RCC patients with BM. Because the pre-RT chemotherapy in the Katagiri scoring system seemed to be influenced by the aggressiveness of hormone-resistant prostate and breast cancers, this factor did not seem to be important for predicting the prognosis of RCC patients with BM. In contrast, abnormal laboratory data and pre-RT TTs had a small impact on the prognosis of RCC patients with BMs as included in the Katagiri scoring system. In this study, only 16.5% (18/109) of the patients had normal laboratory data, and only 7.3% (8/109) had critically abnormal laboratory data. Most patients had abnormal laboratory data, which may have influenced the small impact of abnormal laboratory data on the prognosis of RCC patients with BM in this study.

Specific scoring systems for single cancers are important when considering the individual characteristics of a primary cancer type. In this study, a scoring system was devised for RCC patients with BM. Five factors [ECOG-PS (≥2:1 point), primary site (no control: 1 point), disseminated metastasis (yes: 1 point), lymph node metastasis (yes: 1 point), and number of bone metastatic lesions (multiple: 1 point)] were important in predicting the survival time of patients with BMs from RCC. In addition, two prognostic groups (favorable: 0-1 points and unfavorable: 2-4 points) that were significantly correlated with survival time were devised according to the regression coefficients of these factors. The significance of the RT dose escalation for BMs from RCC is controversial, but the re-irradiation rate is higher in the lower RT dose group (4,9,26,27). Therefore, although a higher RT dose may be preferable in the favorable group (median OS, 19 months), a lower RT dose should be administered aggressively in the unfavorable group (median OS, 5 months). Moreover, some studies have reported that stereotactic body radiation therapy (SBRT), a precise irradiation technique with an extremely

Table III. Points of significant prognostic factors.

Characteristic	Point
ECOG-PS	
≥2	1
<2	0
Primary site	
No control	1
Control or de novo	0
Disseminated metastasis	
Yes	1
No	0
Lymph node metastasis	
Yes	1
No	0
Number of bone metastatic lesions	
Multiple	1
Single	0

ECOG PS, Eastern Cooperative Oncology Group Performance Status.

Table IV. Associations between the total points, and 0.5- and 1-year OS rate.

Total points	n	0.5-year OS rate, %	1-year OS rate, %
0	16	100	100
1	31	89.7	85.7
2	40	67.3	34.3
3	18	44.4	37.0
4	4	25.0	0

OS, overall survival.

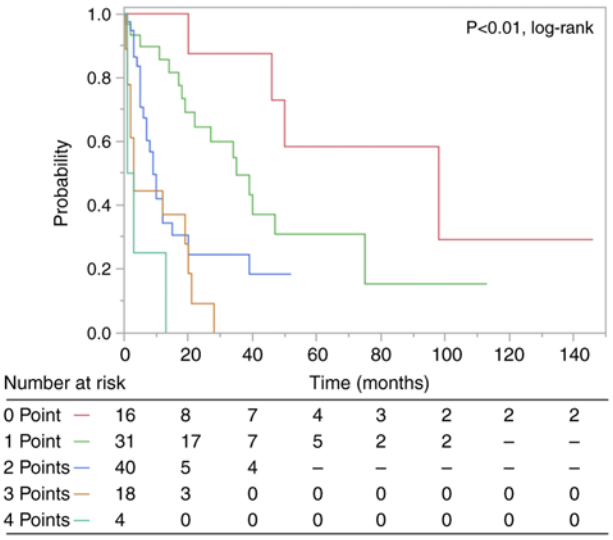

Figure 2. Kaplan-Meier curves of survival rates in RCC patients with bone metastases according to different scores. In RCC patients with bone metastasis, the total point score of 2-4 was correlated with unfavorable prognosis. RCC, renal cell carcinoma.

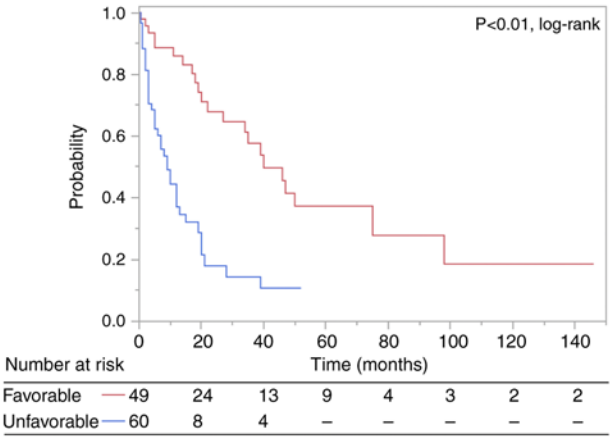

Figure 3. Kaplan-Meier curves of survival rates in RCC patients with bone metastases according to total point scores of 0-1 (favorable) and 2-4 (unfavorable). In RCC patients with bone metastasis, the favorable group (total point score 0-1) had a significantly better survival rate than the unfavorable group (total point score 2-4) (P<0.01, log-rank test). RCC, renal cell carcinoma.

high dose per fraction, has remarkably improved local control of primary and metastatic RCC (28-30). In Japan, SBRT for spinal metastases or oligometastases has been available in routine clinical practice under the Japanese National Health Insurance System since April 2020. However, currently, the number of patients treated with SBRT for spinal metastases or oligometastases at our institutions is very small, and no patients has been performed for BMs from RCC. In the future, SBRT may become an option over conventional higher RT doses for the patients in the favorable group.

There are some limitations to our study owing to its retrospective nature. First, the number of patients included in this study was relatively small. Therefore, it is possible that visceral metastasis (brain, liver, or lung metastases) may not be an unfavorable prognostic factor. Large-scale prospective studies are needed to validate the findings. Second, our study analyzed almost all important factors with reference to the Katagiri scoring system. However, the pathological grade, identified as important for predicting the prognosis of RCC patients with BM (24), could not be examined because of insufficient data. In this study, only 20 cases (grade 1, n=7; grade 2, n=6; grade 3, n=7) could be evaluated for pathological grade. However, in some cases, these data may not be described in routine clinical practice. In addition, although the histological type could not be evaluated in this study because most patients [92.7% (101/109)] had clear cell cancer, important results are useful in daily clinical practice because the majority of RCC were clear cell cancer. Third, our scoring system cannot be accurately compared with the IMDC and MSKCC scoring systems, which are well-known prognostic scoring systems for metastatic RCC. This was not only owing to the lack of detailed laboratory data (neutrophil count) used in the IMDC scoring system but also because of the lack of time from diagnosis of RCC used in the IMDC and MSKCC scoring systems in some patients who were referred

from other hospitals only for palliative RT. With regard to the lack of detailed laboratory data, detailed information is needed because the laboratory data used in the IMDC or MSKCC scoring systems are used to determine optimal treatment strategies. In contrast, in patients referred to radiation oncologists for palliative RT, minimal laboratory data are often obtained. This difference in the purpose of examinations may have influenced the collected laboratory data. Furthermore, the laboratory data for the Katagiri scoring system, which was used as a reference in devising our scoring system, showed abnormal C-reactive protein levels in most patients (67.9%, n=74). In addition, the laboratory data for the MSKCC scoring system showed abnormal hemoglobin values in most patients (77.1%, n=84). This indicates that abnormal laboratory data were observed in many patients who received palliative RT, regardless of the scoring system used. Therefore, abnormal laboratory data may be important for predicting the prognosis of bone metastatic RCC; however, it was unlikely to emerge as an important factor in our study. With regard to the time from RCC diagnosis, the date of RCC diagnosis was unknown in some patients who were referred to radiation oncologists for palliative RT from other hospitals, but the MSKCC scoring system could be used if these patients were assumed to be in the group of time from diagnosis to therapy initiation ≥1 year. However, the prognostic classification using the MSKCC scoring system based on this hypothesis was less optimal than our prognostic scoring system (Figs. S1 and S2). Therefore, we believe that our prognostic scoring system may be more useful for radiation oncologists compared to the MSKCC scoring system for selecting optimal RT doses. Finally, because this was a long-term, multicenter, retrospective study, detailed information on the reasons for selecting the RT schedule, palliative effects of treatment, and adverse events was difficult to obtain. A higher RT dose may be prescribed for some degree of local control even if pain control is the main purpose of palliative RT. Owing to these limitations, further large-scale studies based on more detailed information are required.

We have devised a new scoring system for patients with bone metastases from RCC. Our prognostic model for RCC patients with BMs may be useful for selecting an appropriate RT dose.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

KM designed the study concepts. KM, YH, HK, KN, YK and TK collected patient data. KM and YH analyzed data. KM, YH, HK, KN, YK and TK drafted the article. KM, YH, HK, KN, YK and TK collaborated in the discussion. KM prepared the manuscript and YH edited the manuscript. KM and YH confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

All procedures in studies involving human participants were performed in accordance with the ethical standards of the institutional research committee, and The 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. The need for patient consent was waived by the institutional ethics committee due to the retrospective nature of the study.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Coleman RE: Metastatic bone disease: Clinical features, pathophysiology and treatment strategies. Cancer Treat Rev 27: 165-176, 2001.
2. Tsuya A, Kurata T, Tamura K and Fukuoka M: Skeletal metastases in non-small cell lung cancer: A retrospective study. Lung Cancer 57: 229-232, 2007.
3. Svensson E, Christiansen CF, Ulrichsen SP, Rørth MR and Sørensen HT: Survival after bone metastasis by primary cancer type: A Danish population-based cohort study. BMJ Open 7: e016022, 2017.
4. Rades D, Walz J, Stalpers LJA, Veninga T, Schulte R, Obralic N, Wildfang I, Engenhart-Cabilic R, Hoskin PJ and Schild SE: Short-course radiotherapy (RT) for metastatic spinal cord compression (MSCC) due to renal cell carcinoma: Results of a retrospective multi-center study. Eur Urol 49: 846-852, 2006.
5. Chow R, Hoskin P, Schild SE, Raman S, Im J, Zhang D, Chan S, Chiu N, Chiu L, Lam H, *et al*: Single vs multiple fraction palliative radiation therapy for bone metastases: Cumulative meta-analysis. Radiother Oncol 141: 56-61, 2019.
6. Rades D, Lange M, Veninga T, Stalpers LJ, Bajrovic A, Adamietz IA, Rudat V and Schild SE: Final results of a prospective study comparing the local control of short-course and long-course radiotherapy for metastatic spinal cord compression. Int J Radiat Oncol Biol Phys 79: 524-530, 2011.
7. Rades D, Segedin B, Conde-Moreno AJ, Garcia R, Perpar A, Metz M, Badakhshi H, Schreiber A, Nitsche M, Hipp P, *et al*: Radiotherapy with 4 Gy x 5 versus 3 Gy x 10 for metastatic epidural spinal cord compression: Final results of the SCORE-2 trial (ARO 2009/01). J Clin Oncol 34: 597-602, 2016.
8. Makita K, Hamamoto Y, Kanzaki H, Kataoka M, Yamamoto S, Nagasaki K, Ishikawa H, Takata N, Tsuruoka S, Uwatsu K and Kido T: Local control of bone metastases treated with external beam radiotherapy in recent years: A multicenter retrospective study. Radiat Oncol 16: 225, 2021.
9. Makita K, Hamamoto Y, Kanzaki H, Nagasaki K, Takata N, Tsuruoka S, Uwatsu K and Kido T: Factors affecting local control of bone metastases from radioresistant tumors treated with palliative external beam radiotherapy. Discov Oncol 14: 74, 2023.
10. Katagiri H, Okada R, Takagi T, Takahashi M, Murata H, Harada H, Nishimura T, Asakura H and Ogawa H: New prognostic factors and scoring system for patients with skeletal metastasis. Cancer Med 3: 1359-1367, 2014.
11. Bollen L, van der Linden YM, Pondaag W, Fiocco M, Pattynama BP, Marijnen CA, Nelissen RG, Peul WC and Dijkstra PD: Prognostic factors associated with survival in patients with symptomatic spinal bone metastases: A retrospective cohort study of 1,043 patients. Neuro Oncol 16: 991-998, 2014.

12. Westhoff PG, de Graeff A, Monninkhof EM, Bollen L, Dijkstra SP, van der Steen-Banasik EM, van Vulpen M, Leer JW, Marijnen CA and van der Linden YM; Dutch Bone Metastasis Study Group: An easy tool to predict survival in patients receiving radiation therapy for painful bone metastases. Int J Radiat Oncol Biol Phys 90: 739-747, 2014.
13. Willeumier JJ, van der Linden YM, van der Wal CWPG, Jutte PC, van der Velden JM, Smolle MA, van der Zwaal P, Koper P, Bakri L, de Pree I, *et al*: An easy-to-use prognostic model for survival estimation for patients with symptomatic long bone metastases. J Bone Joint Surg Am 100: 196-204, 2018.
14. Escudier B, Eisen T, Stadler WM, Szczylik C, Oudard S, Siebels M, Negrier S, Chevreau C, Solska E, Desai AA, *et al*: Sorafenib in advanced clear-cell renal-cell carcinoma. N Engl J Med 356: 125-134, 2007.
15. Motzer RJ, Hutson TE, Tomczak P, Michaelson MD, Bukowski RM, Rixe O, Oudard S, Negrier S, Szczylik C, Kim ST, *et al*: Sunitinib versus interferon alfa in metastatic renal-cell carcinoma. N Engl J Med 356: 115-124, 2007.
16. Motzer RJ, Hutson TE, Tomczal P, Michaelson MD, Bukowski RM, Oudard S, Negrier S, Szczylik C, Pili R, Bjarnason GA, *et al*: Overall survival and updated results for sunitinib compared with interferon alfa in patients with metastatic renal cell carcinoma. J Clin Oncol 27: 3584-3590, 2009.
17. Sternberg CN, Davis ID, Mardiak J, Szczylik C, Lee E, Wagstaff J, Barrios CH, Salman P, Gladkov OA, Kavina A, *et al*: Pazopanib in locally advanced or metastatic renal cell carcinoma: Results of a randomized phase III trial. J Clin Oncol 28: 1061-1068, 2010.
18. Motzer RJ, Escudier B, McDermott DF, George S, Hammers HJ, Srinivas S, Tykodi SS, Sosman JA, Procopio G, Plimack ER, *et al*: Nivolumab versus everolimus in advanced renal-cell carcinoma. N Engl J Med 373: 1803-1813, 2015.
19. Heng DY, Xie W, Regan MM, Warren MA, Golshayan AR, Sahi C, Eigl BJ, Ruether JD, Cheng T, North S, *et al*: Prognostic factors for overall survival in patients with metastatic renal cell carcinoma treated with vascular endothelial growth factor-targeted agents: Results from a large, multicenter study. J Clin Oncol 27: 5794-5799, 2009.
20. Heng DY, Xie W, Regan MM, Harshman LC, Bjarnason GA, Vaishampayan UN, Mackenzie M, Wood L, Donskov F, Tan MH, *et al*: External validation and comparison with other models of the international metastatic renal-cell carcinoma database consortium prognostic model: A population-based study. Lancet Oncol 14: 141-148, 2013.
21. Motzer RJ, Bacik J, Murphy BA, Russo P and Mazumdar M: Interferon-alfa as a comparative treatment for clinical trials of new therapies against advanced renal cell carcinoma. J Clin Oncol 20: 289-296, 2002.
22. Makita K, Kanzaki H, Hamamoto Y, Nagasaki K, Kataoka M, Kido T and Ohsumi S: Prognostic assessment of patients who receive radiotherapy for bone metastases from breast cancer. Oncol Lett 25: 188, 2023.
23. Makita K, Hamamoto Y, Kanzaki H, Nagasaki K and Kozuki T: An easy tool to predict survival in patients with bone metastatic lung cancer treated with palliative radiotherapy. Thorac Cancer 14: 1795-1801, 2023.
24. Fan Z, Huang Z and Huang X: Bone metastasis in renal cell carcinoma patients: Risk and prognostic factors and nomograms. J Oncol 2021: 5575295, 2021.
25. Rades D, Haus R, Janssen S and Schild SE: An easy-to-use scoring system to estimate the survival of patients irradiated for bone metastases from lung cancer. Transl Lung Cancer Res 9: 1067-1073, 2020.
26. Rades D, Freundt K, Meyners T, Bajrovic A, Basic H, Karstens JH, Adamietz IA, Wildfang I, Rudat V, Schild SE and Dunst J: Dose escalation for metastatic spinal cord compression in patients with relatively radioresistant tumors. Int J Radiat Oncol Biol Phys 80: 1492-1497, 2011.
27. Freundt K, Meyners T, Bajrovic A, Basic H, Karstens JH, Adamietz IA, Rudat V, Schild SE, Dunst J and Rades D: Radiotherapy for oligometastatic disease in patients with spinal cord compression (MSCC) from relatively radioresistant tumors. Strahlenther Onkol 186: 218-223, 2010.
28. Siva S, Louie AV, Kotecha R, Barber MN, Ali M, Zhang Z, Guckenberger M, Kim MS, Scorsetti M, Tree AC, *et al*: Stereotactic body radiotherapy for primary renal cell carcinoma: A systematic review and practice guideline from the international society of stereotactic radiosurgery (ISRS). Lancet Oncol 25: e18-e28, 2024.
29. Amini A, Altoos B, Bourlon MT, Bedrick E, Bhatia S, Kessler ER, Flaig TW, Fisher CM, Kavanagh BD, Lam ET and Karam SD: Local control rates of metastatic renal cell carcinoma (RCC) to the bone using stereotactic body radiation therapy: Is RCC truly radioresistant? Pract Radiat Oncol 5: e589-e596, 2015.
30. Altoos B, Amini A, Yacoub M, Bourlon MT, Kessler EE, Flaig TW, Fisher CM, Kavanagh BD, Lam ET and Karam SD: Local control rates of metastatic renal cell carcinoma (RCC) to thoracic, abdominal, and soft tissue lesions using stereotactic body radiotherapy (SBRT). Radiat Oncol 10: 218, 2015.