Clinical characteristics and prognosis of renal cell carcinoma with spinal bone metastases

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Abstract

Background: The prognosis of renal cell carcinoma (RCC) with spinal bone metastasis (sBM) varies greatly. To define the clinical characteristics and prognostic factors of RCC with spinal bone metastasis (sBM) in our center.

Methods: The clinical and medical records of RCC patients with sBMs were collected. The gender, age, time of BM, the extent of BM, the number of BMs, the presence or absence of visceral metastasis and the pathological type of BM were investigated. All patients were followed up regularly. OS was calculated from the date of BMs diagnosis to death or last follow-up using Kaplan-Meier method and modelled with Cox regression analysis.

Results: 22 RCC patients with sBM were collected. sBM was found synchronously in 15 patients (68.2%) and metachronously in 7 patients (31.8%) . The median survival time was 30 months in 7 patients (31.8%) with solitary sBM and 19 months in 15 patients (68.2%) with multiple sBMs. Visceral metastasis occurred in 6 patients (27.3%) with the median survival time of 17 months, while the other 16 patients (72.7%) had no visceral metastasis with the median survival time of 29 months ($P = 0.006$). Enblock resection was done in 7 patients with median survival time of 34 months. Non-Enblock resection were done in 15 patients with median survival time of 18 months($P = 0.006$). Multivariate COX regression analysis showed that visceral metastasis and Enblock resection are the independent prognostic factors of RCC with sBM.

Conclusions: No visceral metastasis, En-block resection are good prognostic factors for RCC with sBM. Therefore En-block resection of sBM is recommended for RCC without visceral metastasis.

Background

Renal cell carcinoma (RCC) accounts for 2%–3% of all adult malignant neoplasms. Its incidence predominates in men, with the male-to-female ratio being 1.5:1.0 and peaks at age 60–70 years. The incidence of RCC has increased by an average of 2% per year[1, 2]. One third of patients with RCC have metastatic lesions at the time of diagnosis, and 20%–40% develop metastatic lesions during the follow-up[3]. The bone is the second most common site of RCC metastasis, and approximately 40% of bony metastases occur in the spine. Spinal bone metastasis (sBM) is considered a negative indicator of overall survival[4]. With present targeted drugs, the proportion of patients achieving an objective response has been between 20%–40%, with complete responses in only 1%–3% of patients[5]. Removal of all synchronous or metachronous lesions, when technically feasible and clinically appropriate, provides the only potentially curative treatment alternative. In order to identify the prognostic factors of RCC patients with sBM and find the suitable patients for surgical treatment to improve their survives as the purpose of this study.

Methods

A total of 22 RCC patients with spinal bone metastasis were collected. They were admitted to the Department of Urology, Bone Oncology and Spine Surgery Beijing Jishuitan Hospital from 2009 to 2018. The clinical and medical records were investigated. The patients were followed up regularly. Inclusion criterion: patients with (1) newly diagnosed sBM from RCC. (2) sBM diagnosed by bone scan or PET-CT. (3) clear pathology diagnosis of the sBM. Exclusion criterion (1) concomitant other malignant neoplasms. (2) without surgical treatment of bone metastasis.

Investigations and follow-up

The gender, age, time of BM, the extent of BM, the number of BMs, the presence or absence of visceral metastasis and the pathological type of BM were investigated. All patients were followed up regularly after surgery with 3 months interval in the first year and 6 months interval thereafter. The patient was received routine laboratory and imaging examinations.

According to the time of BM, patients were divided into two groups: RCC with sBM synchronously group and RCC with sBM metachronously group. According to the extent of BMs, patients were divided into five groups: only sBM, sBM with limb BMs, sBM with ribs or clavicle BMs, sBM with pelvis or iliac BMs, multiple sites BMs.

Statistical Analysis

statistical software SPSS 20.0 was used to process data. The measurement data was expressed in M(range) and the count data was expressed in quantity and percentage. OS was calculated from the date of BMs diagnosis to death or last follow-up using Kaplan-Meier method and modelled with Cox regression analysis. The difference between groups was determined by Lon-rank test. The difference was statistically significant at $P<0.05$.

Results

Clinical characteristics

22 newly diagnosed RCC patients with sBM were collected(Table 1). Among them 19 were male(accounting for 86.4%)and 3 were female (account for 13.6%). The ratio of male to female patients was 6.33:1. The youngest was 45 years old, the oldest was 74 years old and the average age was 57.6 ± 6.9 years

Table 1: Clinical characteristics of newly diagnosed RCC with sBM

	Factors	Cases	Propotion
Gender	Male	19	86.4%
	Female	3	13.6%
Time of sBM	Synchronously	15	68.2%
	Metachronously	7	31.8%
Number of sBMs	Solitary	7	31.8%
	Multiple	15	68.2%
Range of BMs	Only sBM	7	31.8%
	sBM with limb BMs	5	22.7%
	sBM with ribs or clavicle BMs	2	9.1%
	sBM with pelvis or iliac BMs	6	27.3%
	Multiple sites BMs	2	9.1%
Visceral Metastasis	Yes	6	27.3%
	No	16	72.7%
Resection of BMs	En-block	7	31.8%
	Non-En-block	15	68.2%
Pathology Type	Clear Cell Carcinoma	21	95.5%
	Non Clear Cell Carcinoma	1	4.5%

sBM was found synchronously in 15 patients (68.2%)and metachronously in 7 patients(31.8%). In RCC patients with sBM metachronously , the shortest time for the occurrence of sBM was 3 months, the longest time was 108 months and the median time was 14.2 months. According to the number of sBMs, 7 patients (31.8%)had solitary sBM and 15 patients (68.2%)had multiple sBMs. According to the extent of sBM,7 patients (31.8%)had the only sBM, 5 patients (22.7%)had sBM with limb BMs. 2 patients (9.1%)had sBM with ribs or clavicle BMs. 6 patients (27.3%)had sBM with pelvis or iliac BMs. 2 patients (9.1%)had multiple sites BMs.

Visceral metastasis occurred in 6 patients (27.3%), while the other 16 patients (72.7%) had no visceral metastasis. The most common visceral metastasis was lung metastasis in 5 patients(83.3%) followed by the adrenal metastasis in 2patients, retroperitoneal lymph nodes metastasis in 1 patient and Liver metastasis in 1 patient. The most common pathological type was clear cell carcinoma in 21 patients (95.5%)and the Epithelioid differentiation cancer was confirmed in 1 patient(4.5%).

Prognosis analysis

22 patients were followed up for 9-48 months, with a median follow-up of 23 months. A total of 19 patients (86.4%) died at the last follow-up. The median overall survival time of the patients was 22 months, as shown in Figure 1. The median survival time was 22 months and 24 months in the RCC with sBM synchronously group and metachronously group respectively, but the difference between the two groups was not statistically significant($P=0.904$). The median survival time was 30 months and 19 months in the solitary sBM group and multiple sBM group respectively. There was no significant difference between the two groups($P=0.091$).

The median survival time was 34 months in the only sBM group, 29months in the sBM with limb BMs group, 19months in the sBM with ribs or clavicle BMs group, 10months in the sBM with pelvis or iliac BMs group and 11 months in the multiple sites BMs group respectively. The difference between these groups was statistically significant ($P=0.012$). The median survival time was 17 months and 29months in the visceral metastasis group and non-visceral metastasis group respectively. The difference between the two groups was statistically significant($P=0.006$). The median survival time was 34 months and 18 months in the Enblock resection group and non-Enblock resection group respectively. The difference between the two groups was statistically significant($P=0.006$). Multivariate COX regression analysis showed that visceral metastasis and Enblock resection are the independent prognosis factors of RCC patients with sBM, as shown in Table 2.

Table2 COX multivariate regression: survival analysis of RCC with sBM

Variable	<i>P</i> value	HR(95%CI)
Time of SBM	0.554	0.229-2.205
Number of sBMs	0.924	0.153-5.507
Range of BMs	0.185	0.851-2.309
Visceral Metastasis	0.026	0.012-0.899
Enblock Resection	0.046	0.032-0.972

Discussion

The prognosis of RCC with sBM varies greatly. there are many influencing factors [6, 7]. This study focused on prognostic factors associating with the BM, such as the number of sBM, the extent of sBM and the surgical approach of sBM.

The extent of BMs is closely related to the prognosis of RCC patients. Tatsui retrospectively analyzed the prognosis factors of RCC with sBM. The study showed that patients whose spine was the only site of

metastasis had a median OS of 19 months (95%CI 9.8–28.2 months) after surgery, significantly longer than the 9.7 months (95% CI 8.1–11.3 months) observed in patients with additional extraspinal metastasis sites ($p < 0.001$) [8]. Haruki and Fukushima's study also found that the extent of BM affects patients' prognosis[9, 10]. In this study, the median survival time was 34 months in the only sBM group, 29months in the sBM with limb BMs group, 19months in the sBM with ribs or clavicle BMs group, 10months in the sBM with pelvis or iliac BMs group and 11 months in the multiple sites BMs group respectively. The difference between these groups was statistically significant($P = 0.012$). therefore the more extensive of BM, the worse the prognosis of RCC patients. These may be related to the poor general condition of patient with extensive BMs, low tolerance to surgery, and the difficulty of removed all the BMs.

Visceral metastasis such as liver metastasis, lung metastasis are the poor prognostic factor for the RCC with sBM. Yutaka took investigation to 50 patients with BM from RCC—univariate and Cox multivariate regression analysis show that visceral metastasis is the poor prognostic factor for RCC with BM[11]. Ruatta took a large scale single center prognosis study on 300 patients with BM from RCC and found that the OS of patients with visceral metastasis was significant shorter than patients without visceral metastasis(17.6 months vs 46.4months— $P < 0.0001$)[12]. In this study, 6 patients had visceral metastases, with a median survival time of 17 months and 16 patients had no visceral metastases, with the median survival time was 29 months. The difference between the two groups was statistically significant ($P = 0.012$). Therefore, The prognosis of RCC patient with visceral metastasis is very poor. For these patients, palliative symptomatic treatment, to improve the quality of life, should mainly be used.

The surgical approach of BM affects the prognosis of RCC patients with BM. Langerhuizen assessed the local cancer recurrence rate between patients who received stabilization only, intralesional curettage and metastasectomy for RCC metastasis to the appendicular bone. 183 patients were included in the study, the stabilization was done in 22% patients, 30% patients received intralesion curettage and 48% patients underwent resection of BM. The recurrence rate differed and was 39% after stabilization only, 22% after intralesional curettage and 12% after metastasectomy ($P = 0.003$). Patients who received metastasectomy had better survival ($P = 0.020$) [13]. These results were confirmed by SATOSHI KATO's study. 36 RCC patients received nephrectomy and complete resection of solitary spinal lesion. The estimated median CSS time was 130 months, with the 3, 5 and 10 years CSS rates 77.8%, 69.1% and 58% respectively. Patients survival was significantly prolonged after curative resection of solitary spinal metastases [14]. In this study, 7 patients underwent En-block resection of the BM, with a median survival time of 34 months. 15 patients underwent non-Enblock resection of the BM, with a median survival time of 18 months. The differences between these two groups were statistically significant($P = 0.006$). En-block resection of the sBM can prolong the survival time of RCC patient. En bloc spondylectomy is difficult to perform because of the special location of the spine. Improvements in surgical techniques and preoperative embolization in the past two decades achieved excellent clinical results with low morbidity[15, 16]. En bloc spondylectomy has been applied for treating spinal metastasis from a variety of tumors including the RCC[17, 18].

This study initially analyzed the prognostic factors of RCC with sBM. Select bias may exists due to the fewer recruited patients. So large- scale multiple center investigation study is needed in the future to verify it. RCC patients with sBM should be screened according to the clinical factors or even the pathologic and biomaterial factors.No visceral metastasis, En-block resection are good prognostic factors. Therefore En-block resection of sBM is recommended for RCC with sBM to improve their survives.

Conclusions

In conclusion, no visceral metastasis, En-block resection are good prognostic factors for RCC with sBM. Therefore En-block resection of sBM is recommended for RCC without visceral metastasis. However, further large-scale, prospective, and multi-center studies are needed to establish a definite conclusion.

Abbreviations

RCC: renal cell carcinoma; BM: bone metastasis; sBM: spinal bone metastasis

Declarations

Acknowledgements

Not applicable

Author's contributions

JZ: Protocol/project development, Data management, Manuscript writing. NL:Protocol/project development, Data management, Statistical analysis, Manuscript writing. HW: Data Collection, Data analysis. HDW: Data Collection,Data analysis. GH: Critical revision of the manuscript for scientific and factual content, Manuscript editing LM: Critical revision of the manuscript for scientific and factual content, Manuscript editing. All authors read and approved the final version of the manuscript.

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Availability of data and materials

All the data supporting our findings is contained in the manuscript. The datasets used and/or analysed in the current study is available from the corresponding author on reasonable request.

Ethics approval and consent to participate

We verbally inform patients about the purpose of the study and the use of the data in a concise and understandable manner, and promise that all personal information collected will be kept confidential. This study was approved by the Beijing Jishuitan Hospital Local Ethics Committee.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interest

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Figures

Figure 1

Kaplan-Meier estimates of RCC patients survival according to time of sBM(B), number of sBM(C), extent of sBM(D), visceral metastasis(E) and En-block resection(F)