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Original

Long bone metastases as predictors of survival in patients with metastatic renal cancer

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Abstract

BACKGROUND: The aim of this study was to assess the prevalence of long bone metastases in renal cancer patients and to evaluate their utility as predictors of survival in this group.

MATERIAL AND METHODS: This retrospective study included 20 patients with metastatic renal cancer and bone metastases. The patients were referred for regular bone scintigraphy in order to assess disease spread in the skeleton. The patients were divided into two groups: those with 1) metastases in the skeleton (including long bones) and those with 2) metastases in the axial skeleton only.

RESULTS: Bone scintigraphy imaging was performed regularly up to 81 months from the first positive bone scan. During that time 11 deaths (8 among patients with long bone lesions) were recorded. Kaplan-Meyer curves showed that patients with long bone metastases tend to have lower survival probability in comparison to the ones with metastases in other bones.

CONCLUSIONS: Bone metastases localization seems to influence survival in patients with renal cancer. Long bone-involving spread of the disease is associated with worse survival probability than the spread to the other bones.

KEY words: renal cancer, bone metastases, survival, prognostic factor

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Background

Renal cancer is the 7th most common cancer in Poland, accounting for around 4% of all new cases in males and 3% in females. In 2010 in Poland renal cancer was diagnosed in over 2700 men and 1900 women [1]. The overall 5-year survival rate is approximately 45% [2]. However, it strongly depends on the stage of the disease at the moment of diagnosis — it reaches 80% in patients with localized disease and is as low as 12% in those with metastases [3].

Although renal cancer can be highly curable if detected at an early stage, approximately one-third of patients present with locally advanced or metastatic disease at the moment of diagnosis [4]. In another third of patients, metastatic disease appears later following nephrectomy [2]. Renal cancer usually spreads to the lung (75%), soft tissue (36%), bone (20%), liver (18%) and central nervous system (8%) [3, 5].

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The prognosis for patients with bone metastases is considered to be poor, with an average life expectancy of 12–24 months [6]. After pelvis, extremities are the second most common localization of osseous metastatic lesions in renal carcinoma [6, 7]. However, the data on the prognostic value of long bone metastases are scarce and inconsistent.

The aim of the study was to assess the prevalence of long bone metastases in renal cancer patients and to evaluate their utility as predictors of survival in this group.

Materials and methods

This retrospective study included 20 renal cancer patients with bone metastases who underwent a series of bone scintigraphy examinations.

Bone scintigraphy studies were acquired using dual-head hybrid SPECT-CT cameras (Infinia VC Hawkeye 1 or Infinia VC Hawkeye 4, General Electric Healthcare). Whole body planar images (low energy high resolution collimator, 256 × 256 matrix, 200 s per projection, 140 kV) were performed 2.5–3 hours after 740–925 Mbq of 99mTc-methylene diphosphonate was injected. The acquisition time was 18–20 minutes.

Table 1. Comparison of patients with and without long bone metastases

	Patients with long bone metastases (n = 10)	Patients without long bone metastases (n = 10)	Significance
Age [± SD]	55 (± 11,6)	60.9 (±11)	ns
Women	5 (50%)	7 (70%)	ns
Men	5 (50%)	3 (30%)	ns
Total no. of metastases (mean) [± SD]	8.1 (±5)	2.3 (±1.9)	$p < 0.01$
Deaths	8 (73%)	3 (27%)	$p < 0.05$

Table 2. Comparison of dead and surviving patients

	Dead patients	Surviving patients	Significance
Age [± SD]	54.5 (±10)	62.3 (±12)	ns
Women	5	7	ns
Men	6	2	ns
Total no. of metastases (mean) [± SD]	7.2 (±5.4)	2.7 (±2.3)	$p < 0.04$
Presence of long bone metastases	8	2	$p < 0.03$
No. of long bone metastases (mean) [± SD]	1.3 (±1.4)	0.3 (±0.7)	$P < 0.05$

Depending on the localization of bone metastases the patients were divided into group with 1) metastases in the skeleton including long bones or with 2) metastases in the axial skeleton only. Statistical analysis was performed using t-Student test and Mann-Whitney test. Localization-specific survival probability was estimated using Kaplan-Meyer curves.

Results

The study included 20 patients (10 men and 10 women) aged 33–91 years (mean ± SD: 62 ± 19.7 years). Each patient had metastatic renal cancer with osseous lesions. The patients were followed-up for 4–81 months since the first bone scintigraphy imaging. Eleven deaths (including 8 among patients with long bone lesions) were recorded from the moment of disease diagnosis to 60 months of follow-up. Long bone metastases were observed in 10/20 patients (50%). The mean number of bone metastases was significantly higher in patients with long bone lesions (8.1 vs 2.3, $p < 0.01$) (Table 1).

We observed that patients who were alive at the end of the follow-up period had lower total number of metastases as well as long bone lesions — 2.7 vs 7.2 ($p < 0.04$) and 0.3 vs 1.3 ($p < 0.05$) respectively. The mean age of patients who were alive at the end of the follow-up period was higher than in the patients who died during observation (62.3 vs 54.5 years). However, the difference was not statistically significant (Table 2).

Kaplan-Meyer curves, drawn in order to estimate survival probability depending on bone metastases localization, show that patients with long bone metastases tend to have lower survival probability than the ones with metastases in the axial skeleton (Fig. 1).

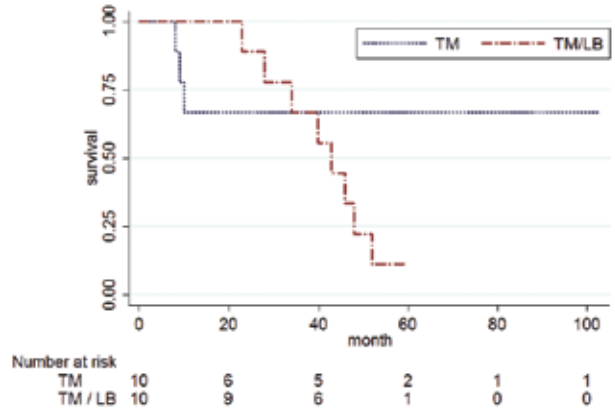

Figure 1. Kaplan-Meyer survival probability curves. Patients with long bone metastases tend to have lower survival probability than the patients with metastases observed in other bones; TM — axial skeleton metastases, TM/LB — axial and appendicular skeleton metastases

Discussion

The most significant prognostic factors in renal cancer patients seem to be the stage, tumour size, Fuhrman grade of primary tumour, patient condition, presence of metastases and their location [8, 9].

Our data indicates that patients with long bone metastases tend to have lower survival probability than the patients with metastases observed in other bones. Additionally, the patients with long bone metastases have more osseous lesions in total. We also observed that the patients who died during the follow-up period were younger and had higher number of osseous lesions, including long bone metastases. Yet, the authors are of the opinion that precise assessment of incremental predictive value of long bone metastases in metastatic renal cancer requires larger group of patients.

The data on the prognostic value of long bone metastases are scarce. According to Althausen et al. [6] who studied 38 cases of metastatic renal cell carcinoma with secondary osseous metastases there were two factors that appeared highly statistically significant in predicting survival — the site of bone metastases and the time from renal cancer diagnosis to the first metastasis. The authors observed that the outcome was significantly worse if first bone lesions appeared in the axial skeleton, and especially the

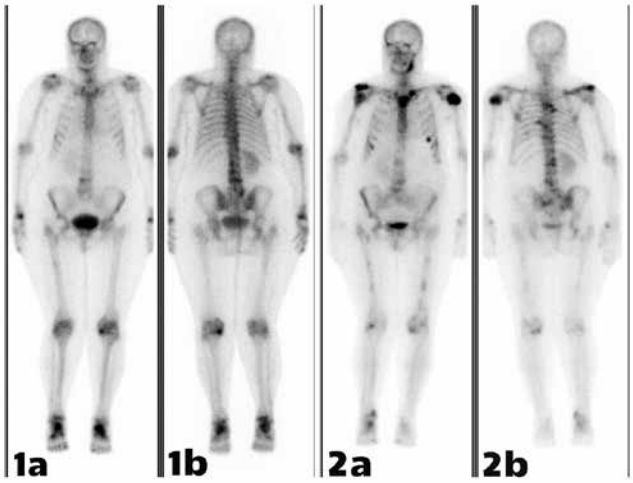

Figure 2. Bone scintigraphy scans in a 64-year-old patient. The first positive bone scan (1a, 1b) shows multiple osseous lesions limited to the spine. The last bone scintigraphy (performed 2 months before the patient's death) revealed disseminated bone metastases both in the axial and the appendicular skeleton (2a, 2b). The patient was followed--up for 46 months

pelvis, than if they occurred in the extremity bones (femur, tibia and humerus). A worse survival rate was also shown for patients with early onset of metastases. Survival for the entire series was 90% at 6 months, 84% at 1 year, 55% at 5 years and 39% for 10 years.

In our study the data on the localisation of first metastatic bone lesions was unavailable as the patients were not followed-up from the time of renal cancer diagnosis but from the first scintigraphic examination (which was positive for bone metastases in all patients). However, contrarily to Althausen et al. [6] our data suggests that patients with both appendicular and axial skeleton lesion have significantly worse survival prognosis than the patients with axial skeleton lesions only (Fig. 2). We also observed that the patients with long bone lesions had significantly higher total number of bone metastases than the patients with axial skeleton lesions — the mean was 8.1 and 2.3 respectively ($p < 0.01$) (Table 1).

The literature search also yielded studies that did not show correlation between bone metastases localization and survival. Dineen et al. [10] found that metastasis site did not influence survival. The study, however, assessed survival in patients after surgical excision of a solitary metastasis from renal carcinoma. Out study, to the contrary, included patients with disseminated osseous lesions.

Retrospective study by Szendröi et al.[4] including 65 renal clear cell carcinoma patients operated for bone metastases showed that the lesion localization in the skeleton did not correlate with the survival neither after renal ($p = 0.1787$) nor after bone surgery ($p = 0.4786$). The assessed group of patients did not, however, include patients with spine metastases which seem to negatively influence the survival prognosis.

Conclusions

Long bone metastases localization may influence survival in patients with renal cancer. The incremental prognostic value of long bone metastasis needs to be confirmed in larger trial.

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