

Surgical Treatment of Osseous Metastases in Patients With Renal Cell Carcinoma

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Forty-five patients who underwent surgical treatment for osseous metastases secondary to renal cell carcinoma between 1980 and 1998 were reviewed. The diagnosis was confirmed histologically in all patients. The mean age of the 34 men was 61.5 ± 9 years and of the 11 women 55.2 ± 17.6 years. The most common locations of the metastases were the spine (15 patients), the pelvis (eight patients), and the femur (11 patients). In 21 patients, the renal cell carcinoma was diagnosed when the osseous metastasis was detected. The time from diagnosis of the primary tumor to metastasis in the remaining patients ranged from 0 to 23 years (mean, 3 ± 5 years). At presentation, 19 patients had a singular lesion. Nine patients had multiple osseous metastases and 17 patients had additional visceral involvement. In seven

patients, a wide or radical resection was done; in 35 patients, a palliative procedure was done; and in three patients, only a diagnostic procedure was done. For the whole group, the survival was 49% after 1 year, 39% after 2 years, and 15% after 5 years. Only the extent of the disease and the latency period between primary tumor diagnosis and first detection of osseous metastasis could be identified as independent factors of survival. Nine patients with solitary metastasis to the bone more than 12 months after resection of the primary tumor showed a 5-year survival of 54%.

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Renal cell carcinoma is one of the most common malignancies observed. The American Cancer Society estimated the number of cases in 1996 to be 30,000.⁵ Depending on the series, 20% to 50% of these patients have distant metastasis at presentation.^{4,19,22} The most common site of metastasis is the lung, in approximately 50% of patients, and the second most common site is the skeleton, in approximately 20% to 40% of patients.^{4,13}

Osteolytic bone destruction is caused by secondary stimulation of osteoclasts by tumor cells.² For patients with skeletal metastases, survival rates of more than 50% after 5 years are reported.¹ Bone metastases cause

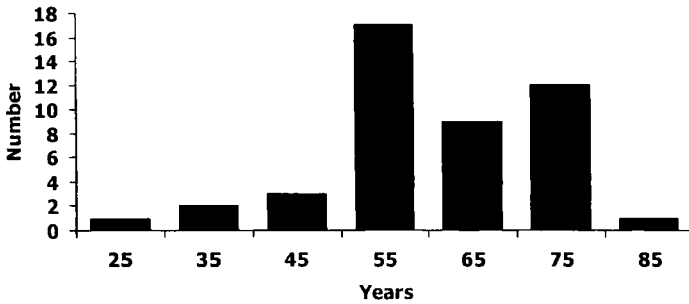


Fig 1. Age distribution of 45 patients with osseous metastases secondary to renal cell carcinoma.

considerable therapeutic problems with respect to the extent of surgical removal, recurrence, and durability of internal fixation. Retrospectively, the data from a consecutive series of 45 patients with renal cell carcinoma who were treated surgically for solitary or multiple metastasis to the bone were reviewed. Improved patient selection is thought to be the most important criterion regarding survival benefits and quality of life. Clinical behavior, surgical procedures, treatment results, and prognostic factors were analyzed.

MATERIALS AND METHODS

Between September 1980 and January 1998, 45 patients with metastases to bone secondary to renal cell carcinoma were treated surgically. The patients' age, gender, treatment of the primary tumor and extraosseous metastases, time of appearance of bone and visceral metastases, clinical presentation, surgical treatment, complications, and survival were analyzed retrospectively.

Statistical analyses were performed using the Cox regression for multivariate analysis, Kaplan-Meier life table analyses, and log rank test for univariate analysis.

The mean age of the 34 men was 61.5 ± 9 years, and the mean age of the 11 women was 55.2 ± 17.6 years (range, 27–84 years) (Fig 1). The sites of the surgical procedures are shown in Figure 2. The most common locations of osseous metastases secondary to renal cell carcinoma were the spine (15 patients), the pelvis (eight patients), and the femur (11 patients). All patients presented with pain; five

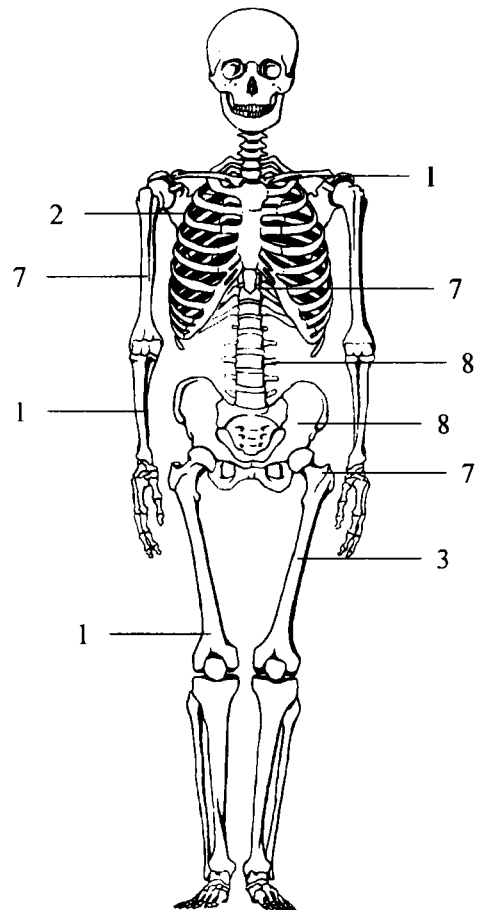


Fig 2. Location of lesions treated surgically in 45 patients with osseous metastases secondary to renal cell carcinoma.

had neurologic impairment, and four had a pathologic fracture of the extremities.

In 21 (47%) patients, renal cell carcinoma was diagnosed when osseous metastases was detected, and in 18 patients, the primary carcinoma was detected because of the metastatic disease.

At presentation 19 patients had a singular osseous lesion. In four of the patients, visceral metastases had been resected previously. Nine patients had multiple osseous metastases (more than one lesion), and 17 patients had additional visceral involvement.

The time from diagnosis of renal cell carcinoma to osseous metastasis ranged from 0 to 23.4 years (mean, 3 ± 5 years; median, 0.57 years). In 60% of the patients, the tumors metastasized in the first year; in 78%, in the first 5 years; and in 89%, in the first 10 years. Only five patients had an interval longer than 10 years free of metastasis (Fig 3).

Surgical treatment in the 45 patients varied greatly because of different tumor locations, extent of disease, the patient's general status, and the long period reviewed. Incisional biopsy only was performed in three patients. In 15 patients with involvement of the spine, nine were operated on only through a dorsal procedure, and in six patients a ventral or a combined procedure was performed. In 12 patients, resection of the tumor and implantation of a tumor endoprosthesis were performed. One patient received a standard hip endoprosthesis. In 11

patients intralesional resection, cementation, and instrumentation were done. In two patients tumor resection without reconstruction was done, and in one patient an intercalary allograft was used. In seven patients a wide total tumor resection was done; in 35 patients a palliative procedure was done; and in three patients only a diagnostic procedure was done, depending on the intent of treatment as determined by surgical margins and the additional extent of disease. Because of the hypervascular nature of the lesions, a preoperative transcatheter embolization was done in five patients.

Adjuvant radiation treatment was administered in 35 patients, with nine patients treated before surgery. Chemotherapy was given in 14 patients; in eight of these patients, the chemotherapy was given before surgery.

Currently, 34 (75.6%) patients are dead of their disease. In the 11 surviving patients, the mean observation period is 41.6 ± 38 months (range, 2–109 months; median, 33 months). Three patients have been observed for less than 12 months.

RESULTS

Complications related to the surgical treatment included three neurologic impairments, two luxations of tumor endoprostheses, one deep infection, one case of insufficiency of the

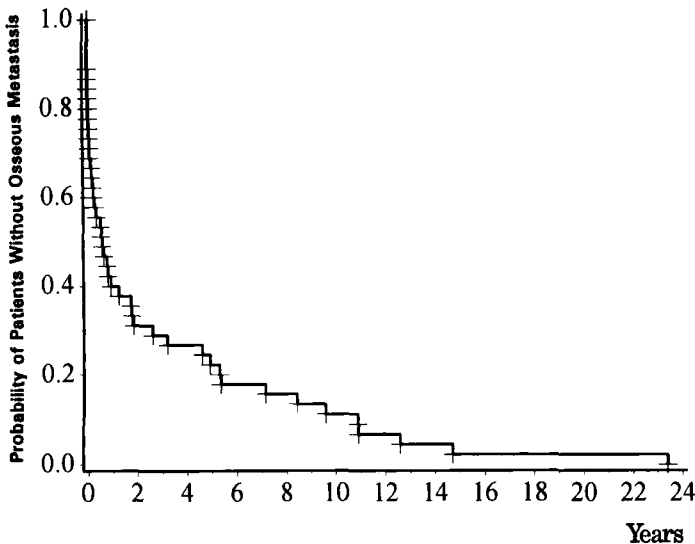


Fig 3. Time from diagnosis of renal cell carcinoma to osseous metastasis in 45 patients.

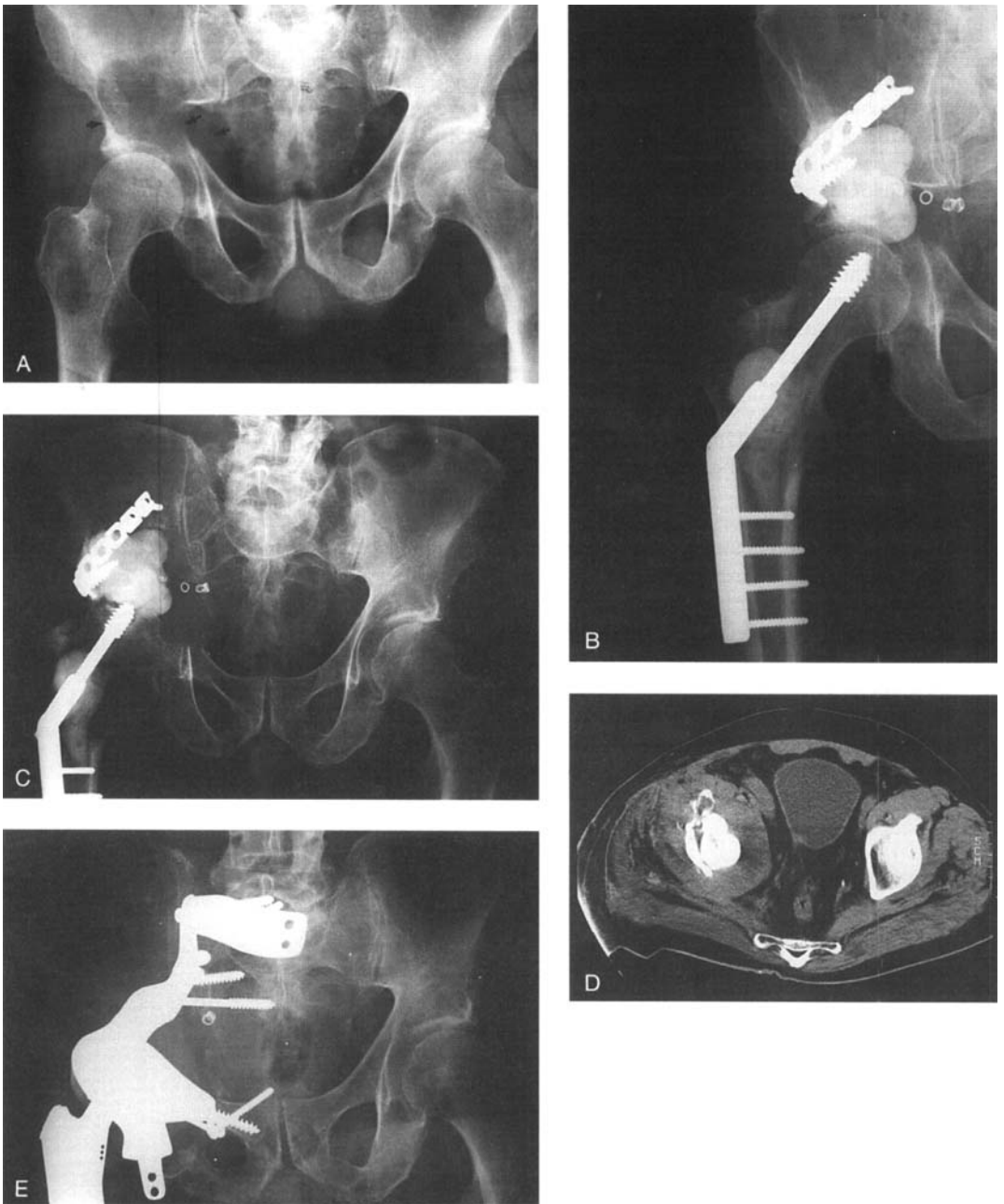


Fig 4A–E. (A) Radiograph of the pelvis of a 71-year-old man obtained 2 months after nephrectomy for renal cell carcinoma showing two osteolytic lesions: one in the right os ileum with huge soft tissue extension (arrows) and the other in the proximal right femur. (B) Radiograph of the right hip in the same patient 2 weeks after curettage, osteosynthesis, and cementation of the metastatic lesions without signs of recurrence. (C) Radiograph of the pelvis obtained 7 months after surgery shows recurrence of the tumor in both locations even though the patient underwent radiation therapy. (D) A huge soft tissue extension of the pelvic tumor can be seen on the computed tomography scan. (E) Radiograph showing internal hemipelvectomy and tumor prosthesis of the proximal femur obtained after wide excision of the recurrent tumor. The patient died of tumor progression 29 months after primary surgery.

remaining kidney, and one case of pneumonia. Five patients had local recurrences or local tumor progression. The recurrences or local tumor progression were seen in two patients with tumor endoprostheses, two patients with cementations (Fig 4), and one patient with dorsal instrumentation of the spine.

For the whole group, the survival was 49% after 1 year, 39% after 2 years, 25% after 3 years, and 15% after 5 years (Fig 5). The factors with the highest predictive value were the involvement of multiple bones or visceral tumor spread (Fig 6). Five-year survival for patients with solitary metastasis to bone was 28%. Only one patient with multiple osseous and pulmonary metastases remains free of tumor 6 years after surgery. The patient's age did not influence the outcome. A significantly better survival was seen in patients presenting with osseous metastases late in their disease (Fig 7).

Regarding the location of the osseous metastases, no difference in survival was seen in the extremity or trunk lesions, even after adjusting for solitary or multiple involvement.

Only two independent factors of survival were identified: they were the extent of the disease and the latency between primary tumor diagnosis and first detection of osseous metastasis (Table 1).

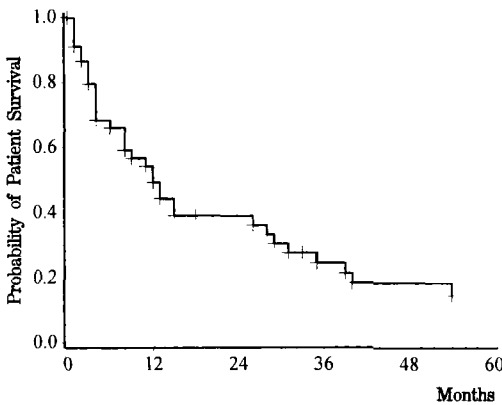


Fig 5. Overall survival in 45 patients who were treated surgically for renal cell carcinoma and osseous metastasis.

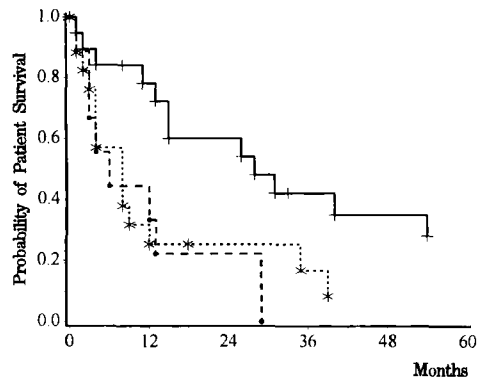


Fig 6. Overall survival in 19 patients with solitary bone metastases (+), nine patients with multiple osseous involvement (●), and 17 patients with additional visceral metastasis (*), $p = 0.014$.

DISCUSSION

The expected survival of patients with metastatic disease of bone is poor. In most patients, palliative and even intralesional procedures are used. Generally, this treatment seems to be justified; however, there are subgroups of patients surviving longer than most patients with metastatic disease.¹⁰ Since the first successful surgical resection in a patient with a solitary pulmonary metastasis in renal cell carcinoma was done, in which the patient survived free of tumor for 23 years,³ a more aggressive approach has been taken in treating metastatic disease. Survival rates of 23%,²¹ 35%,²⁵ 45%,²⁴ and even more than 50% in 5 years are reported.¹ This optimistic view is not supported by the current study and other reports that describe 5-year survival rates of less than 15%.^{11,15-17,19,20} Thus, there is a definite need for a detailed analysis of subgroup treatment and prognostic factors.

Montie et al¹⁷ reported on 14 patients with osseous metastasis only, but none of these patients had radical resection. Smith et al²⁰ also reported on 14 patients, 10 of whom had multiple and visceral metastases, which are indicative of a poor prognosis. Metastatic disease was restricted to the bone in only eight of

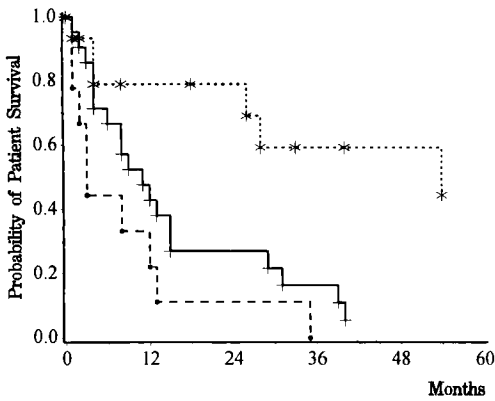


Fig 7. Survival in 15 patients with development of bone metastases more than 12 months (*) after diagnosis of the primary tumor, nine patients with metastases in the first 12 months (+), and 21 patients with initial metastasis (●), $p = 0.001$.

the 181 patients in the study of Maldazys and deKernion.¹⁵ Skinner et al,¹⁹ Giuliani et al,¹¹ and Middleton¹⁶ also reported on patients with extraskeletal tumor involvement, which makes the reported prognosis worse.

The reports showing longer survival times all examined a highly preselected group of patients. In the current study, the 5-year survival rate was 28% in patients with solitary metastasis to bone only. In their study of 586 patients, Tolia and Whitmore²⁵ reported on 12 patients with solitary bone metastasis with a 5-year survival rate of 35%. Three of their patients who were treated with radiation therapy

only and two patients who had local recurrences after primary intralesional surgery had to have amputations later in the course of their disease. Tobisu et al²⁴ studied patients with solitary metastasis to bone resulting in a 5-year survival rate of 37%. The most recent report of Althausen et al,¹ describing patients with a 5-year survival rate of 55%, included 38 patients with skeletal involvement, 16 of whom were treated by wide or radical resection. Most of the discrepancy in survival rates can be explained by the inclusion of patients with different extent of metastatic involvement, the single strongest prognostic factor in numerous series.^{1,7,9,16,19,21,24,25} Only one report indicates that additional extraskeletal involvement does not make the prognosis worse.⁹ Additional osseous tumor spread in known visceral metastases does not worsen patient survival.⁴ What is interesting is the strong negative impact of multiple osseous metastasis without additional organ involvement, as reported by Swanson et al.²¹

The only other significant prognostic factor found in this selected group of patients was the time between diagnosis of the renal cell carcinoma and the first detection of osseous metastasis. This finding also was reported by several other authors.^{15,19,23,24,26} One has to be aware that secondary metastasis might occur more than 20 years after primary treatment. Defining cure as 5- or 10-year tumor free survival may not be justified. Neither the patients' age at the

TABLE 1. Multivariate Analysis of Presumed Factors on Survival in 45 Patients Treated Surgically for Osseous Metastases Secondary to Renal Cell Carcinoma

Factor	Parameter	SE	Risk Ratio	p
Latency*	-0.482	0.219	0.618	0.0277
Tumor spread**	0.493	0.233	1.638	0.0341
Age	-0.011	0.018	0.989	0.5363
Gender	0.331	0.520	1.393	0.5243
Location†	-0.466	0.407	0.627	0.2524
Fracture	0.855	0.740	2.351	0.2478

SE = standard error.

*Initial, < 12 months, \geq 12 months.

**Solitary osseous, multiple osseous or visceral.

†Trunk, extremities.

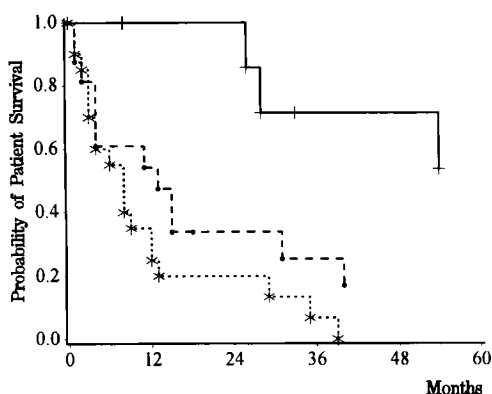


Fig 8. Survival in 45 patients who were treated surgically for osseous metastases secondary to renal cell carcinoma. Nine patients with more than 12 months between diagnosis of the primary tumor and solitary bone involvement (*), 16 patients with either metastasis in the first 12 months or additional organ involvement (●), and 20 patients with early metastasis and additional organ involvement (+), $p = 0.0008$.

time of diagnosis of the primary carcinoma nor the patients' gender was shown to influence survival. There is only one report in the literature indicating a better survival for women with solitary distant renal carcinoma metastasis.¹⁴

As shown in Table 1, a pathologic fracture had no influence on patient survival.¹ However, because of the authors' policy of early surgical treatment to prevent pathologic fractures, only four pathologic fractures were seen in this study group, three of them in patients with multiple metastases.

The location of the tumor, whether in the trunk or in the extremities, also showed no prognostic significance. One report in the literature focuses on this issue in a similar group of patients; however, the total 5-year survival in the patients in that report was twice as high as the rate shown in the current study.¹ This observation might be explained by pretreatment patient selection or by an even more aggressive surgical therapy not applied in the current study at the beginning of the observation period.

The most important strategies in surgical treatment of osseous metastasis in patients with

renal cell carcinoma are radical resection of the lesions resulting in a tumor free status and prevention of recurrences by adequate surgery. Because of the prolonged survival and notoriously poor response to adjuvant treatment modalities, such as radiation therapy, these patients must be treated more aggressively.

Radiation therapy reduces pain from osseous metastasis in nearly all patients, and complete relief of pain was observed in approximately 55% of patients.⁸ The problem is to achieve sclerosis of the osteolytic lesions. Sclerosis of osteolytic lesions was seen in 41 locations treated with more than 30 Gy each.⁶ Sclerosis was achieved immediately after radiation administration in only 0% to 9% of the lesions and 3 months later in only 13% to 33% of the lesions. In another series, 16 of 39 patients had no change, and five had continued tumor growth within the radiation field.¹⁸ Improvement of survival could not be shown.¹²

Two independent factors with significant prognostic value were identified by the authors in the current study: solitary bone involvement and more than 12 months latency between the diagnosis of renal cell carcinoma and detection of bone metastasis. Patients who fulfilled these criteria had a 5-year survival of 54%, patients who fulfilled one criterion had a 5-year survival of 17%, and those with no positive factor had a survival of 0% (Fig 8).

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