Pathol. Oncol. Res. (2010) 16:29–38
DOI 10.1007/s12253-009-9184-7

Prognostic Factors and Survival of Renal Clear Cell Carcinoma Patients with Bone Metastases

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Received: 5 March 2009 / Accepted: 6 July 2009 / Published online: 29 July 2009

Abstract In our retrospective study the pathological and clinical factors, influencing the survival of 65 renal clear cell carcinoma patients operated for bone metastasis between 1990 and 2008 were examined. Based on Kaplan-Meier curves age, gender, clinical symptoms, pathological fracture, progression to the soft tissues, localization and size of the metastasis, whether the occurrence of multiplex metastases is multiorganic or only located to the skeletal system and the stage and grade of primary renal cancer did not influence the survival. The survival significantly improved if the bone metastases were solitary, low Fuhrman grade, late onset; and radical surgery was performed. Based on Cox regression analysis, survival after bone surgery was influenced by the multiplicity and grade of metastasis and by the radicality of the surgery, whereas survival after nephrectomy was significantly influenced by onset time and grade of metastasis. When the solitary metastasis was radically removed, 75.0% of the patients survived the first, and 35.5% the fifth postoperative year. If the metastasis was multiple or the surgery was not radical, no patient survived the fifth year. This is the first report on the prognostic significance of the Fuhrman grade of bone metastasis of renal cell cancer. While the Fuhrman grade of the primary tumour did not influence the survival, the lower grade of metastasis was associated with a significant longer survival. Therefore in cases of solitary, operable, late onset metastases with low Fuhrman grade radical removal is recommended, since this way in 35.5% of cases 5 year survival can be expected.

Keywords Bone metastases · Fuhrman grade · Prognostic factors · Renal cell cancer · Surgical treatment · Survival analysis

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Introduction

Renal clear cell cancer (RCC) runs up to 3% of malignant tumours and more than 50,000 patients are diagnosed with this disease in the United States yearly [1]. At the time of the detection of carcinoma distant metastases are already present in one third of the patients, in another one third metastases appear later, following nephrectomy [2]. The mostly established and widely used clinical and pathological prognostic factors are stage, size, Fuhrman grade of primary tumour, general condition of patient, lack of removal of primary tumour, presence of metastases, the onset time of metastases after nephrectomy and location of metastases [3]. In addition, the RCC gives metastases to the bone system in 20–25% of the cases [2]. The occurrence of the bone metastasis is regarded as a bad prognostic factor as

the life expectancy of patients in this cases is about 12 months, however in a number of cases there are surprisingly long survivals [4]. Successful surgery of solitary metastasis of the RCC was first reported by Barney in 1939 and after the operation, 23 years disease-free survival was recorded [5]. Thereafter, in lack of any efficient treatments (e.g. chemotherapy or radiotherapy), the surgery of bone metastases of RCC came in use. In surgical planning and techniques there are many contradictions observed. On the one hand, related to the commonly disseminated (or disposed to be disseminated) disease and to the short life expectancy, palliative surgeries are suggested by several authors [6]. On the other hand many experts would rather choose radical operations with limited indications based on the longer survival of some patients [7]. The main difficulty is to select candidates for radical surgery.

During our study, the factors influencing the survival of the patients from the aspect of bone metastases surgery were examined. The aim was to offer some assistance for planning and establishing the indication of orthopedic surgeries.

Materials and Methods

During our retrospective assessment the data of 65 patients treated with RCC bone metastases in the Department of Orthopaedics at Semmelweis University between January 1990 and January 2008 were analysed. Renal surgeries were performed at the Urological Department. The patients with vertebral involvement were excluded from our survey. The average age and gender of patients at the time of operation were 61.1±9.7 years (minimum age was 34 and maximum was 79), 50 were male (60.6±9.4 years, 77%) and 15 were female (62.7±10.7 years, 23%).

After nephrectomy, radical removal of the solitary metastases was carried out in 33 patients (group A, 50.8%). Since the metastases could not be removed surgically in 7 cases (10.8%), intralesional resection or excochleation with bone cement were performed (group B). In other 10 cases (15.4%), the metastases were excised radically, however there were further metastases at the time of the operation (group C). In 15 cases (23.0%) only biopsy and transfocal fixation were performed (in order to decrease the pain and help the mobilization), because of the advanced stage and poor general conditions of patients (group D).

Following the different surgical interventions every patient received immunochemotherapy (adhering to the established schemes), which was followed by bisphosphonate treatment.

Two independent pathologists checked the histological diagnosis, the Fuhrman grade, stage of primary tumour and bone metastases retrospectively. The clinical data based on medical documentation, and the results of imaging techniques were collected. When the survival data could not be found in our register, the patients or their relatives were contacted via mail or phone. Moreover our data were compared to data gained from the Central Data Processing Unit of Ministry of Interior. The clinical data of our patients are demonstrated in Table 1.

Statistical Method

At continuous variables the results were given by descriptive method as the sample size, means ± SD and their normality was checked by Leven's test. Statistical analysis was performed using one-way analysis of variance (ANOVA or nonparametric Kruskal-Wallis ANOVA). These were followed by Tukey's test or multiple compar-

Table 1 Categorical variables

Variables	Sample size (N)	Percent values (%)
Male	50	76.9
Female	15	23.1
Symptoms triggered by bone metastases	60	90.8
Pathological fracture	40	61.5
Extracortical invasion	47	72.3
Solitary bone metastasis	40	61.6
Multiplex bone metastases	25	38.4
Peripheral localisation (limbs)	55	84.6
Axial localisation (spine/sacral involvement are excluded)	10	15.4
Radical surgery of solitary bone metastasis (A)	33	50.8
Radical surgery of solitary bone metastasis with positive surgical margin (B)	7	10.8
Locally radical surgery in case of distant metastases (C)	10	15.4
Biopsy/intralesional fixation in case of distant metastases (D)	15	23.0
Primary tumour : Stage 1	18	27.7
Stage 2	7	10.8
Stage 3	9	13.8
Stage unknown	31	47.7
Primary tumour: Grade 1	17	26.1
Grade 2	18	27.7
Grade 3	6	9.2
Grade 4	4	6.2
Grade unknown	20	30.8
Bone metastases: Grade 1	12	18.4
Grade 2	21	32.3
Grade 3	15	23.1
Grade 4	5	7.7
Grade unknown	12	18.5

isons of mean ranks, which was applied, if a significant difference among means was detected. Contingency tables were adapted for categorical variables and Maximum - Likelihood (M-L) Chi-square test or at small sample size Fisher exact test were used to draw the inferences.

Life table methods were used to analyze the survival times. The cumulative survival curves were determined according to the Kaplan-Meier method, with the use of log-rank tests (for pair-wise comparisons and analysis of trend) for statistical assessment. Cox proportional-hazards analysis was used to estimate the prognostic factors.

Differences were considered to be statistically significant at $p<0.05$. All statistical tests were two-sided. Each analysis was performed using the SAS statistical software package (SAS/STAT, Software Release 9.1.3., SAS Institute Inc., Cary , North Carolina 27513, USA).

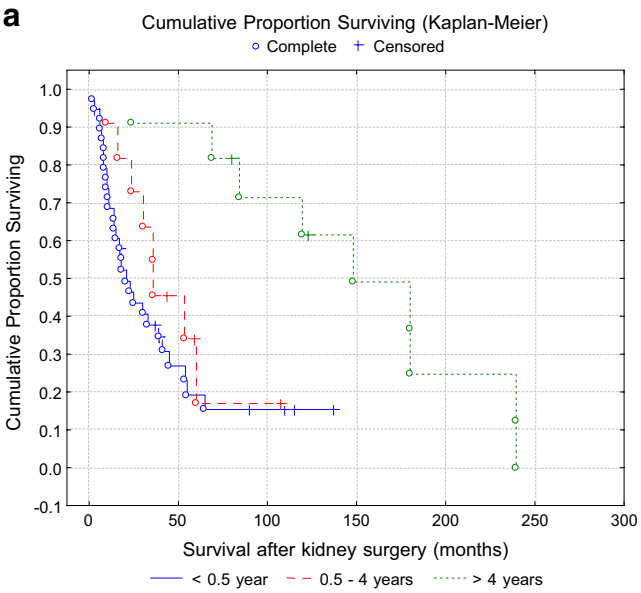
Results

The **age** and the **gender** of the patient did not influence the survival neither after the bone ($p=0.6162$; $p=0.6913$), nor the renal surgery ($p=0.9430$; $p=0.3592$).

The Correlation Between the Survival and the Time Passed From the Nephrectomy Until Recognition of Metastases - Bone metastases were recognised together with the primary RCC in 43 cases (66.1%), while in other 22 cases (33.9%) the detection was after the RCC, with an average latency of 2.1±4.5 years (0.5–19 years). Making a comparison between the survival time after renal surgery and the metastasis onset time after renal surgery, significantly longer survival were experienced at the patients having late onset metachronous metastases (emerged after 4 years), than at patients with synchronous metastases (emerged parallel with the RCC or within 6 months ($p=0.0001$), or at patients with early metastases (emerged half up to four years) ($p=0.0213$). There were no detectable differences between the survival of the synchronous and early metachronous groups ($p=0.2453$) (Fig. 1a). Nevertheless, considering the survival from the operation date of bone metastases, no differences were found among the mentioned groups ($p=0.5001$; $p=0.0949$; $p=0.2161$) (Fig. 1b).

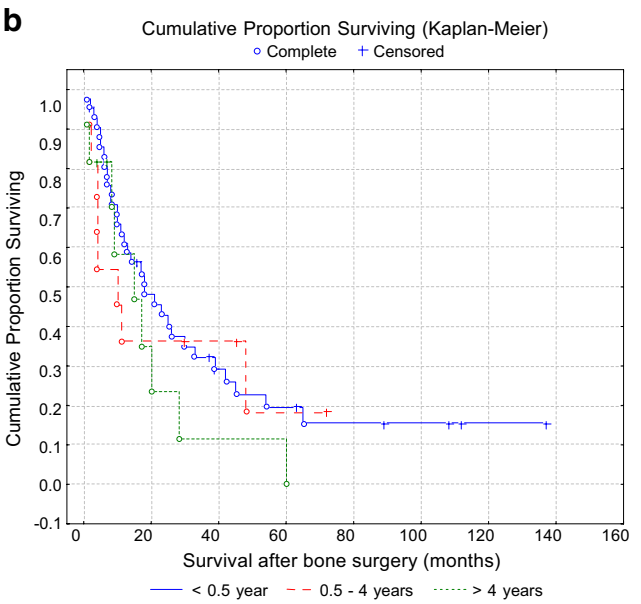
The above mentioned relations were examined, utilizing data from a more homogenous group of patients, who underwent radical surgery of a solitary bone metastasis, excluding other parameters, which might have essential influence on survival as multiplicity and radicality of surgeries. As a result of this survey the same correlations were observed.

The Correlation Between the Symptoms and the Survival - The symptoms caused by the metastasis were local in 85.7% of all cases (pathological fracture, pain, palpable mass) and were general in 14.3% (weight loss, fever, paraneoplastic skin lesions). Although shorter survival could be experienced in the case of general symptoms, the number of those patients was too low to draw correct conclusions.



Late metachron/synchron: p=0.0001; late metachron/early metachron: p=0.0213; early metachron/synchron: p=0.2453

Synchron: n=43
Early metachron: n=11
Late metachron: n=11



Late metachron/synchron: p=0.5001; late metachron/early metachron: p=0.0949; early metachron/synchron: p=0.2161

Synchron: n=43
Early metachron: n=11
Late metachron: n=11

Fig. 1 **a**. Correlation between the onset time of bone metastasis and the survival after kidney surgery. **b** Correlation between the onset time of bone metastasis and the survival after bone surgery

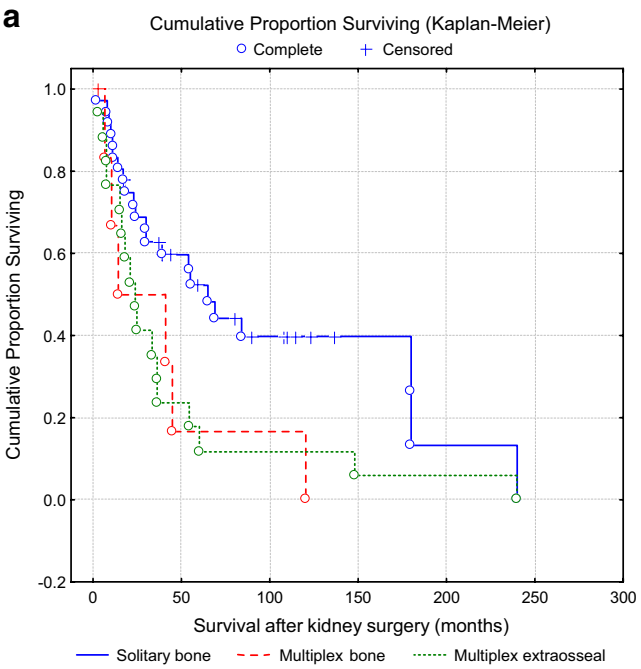
The Relation Among the Pathological Fracture, the Soft Tissue Involvement and the Survival - 40 patients with pathologic fracture were detected (61.5%) and bone metastasis involved the soft tissues in 7 cases (10.7%). The pathological fracture or the soft tissue involvement had no influence neither on the survival after the orthopedic surgery (p=0.6518; p=0.2282), nor on the survival after the nephrectomy (p=0.5170; p=0.9981). Insofar this above mentioned calculation was also made for the patients, who passed the radical removal of solitary bone metastasis; the same results were recorded.

The Coherence Between the Size of the Bone Metastasis and the Survival - According to the pathological reports, the average diameter of the bone metastasis was 9.3± 7.4 cm (min. value 3 cm, max. value 20 cm). The survival neither after the bone, nor after renal surgery showed any coherence with the size of the metastasis (p=0.8777; p= 0.7967). Should one accomplish this comparison only for the patients who had radical surgery of solitary bone metastasis, the published association is also demonstrated.

The Association Between the Solitary and Multiplex Bone Metastasis and Survival - When the orthopedic surgery was performed, 40 patients (61.6%) had solitary and 25 (38.4%) had multiplex metastases. In the case of solitary metastases significantly better survival rate was experienced both for referring to the time of the bone operations (solitary/ multiplex bone: p=0.1762; solitary/ multiplex extraosseal: p=0.0028; multiplex bone/ multiplex extraosseal: p= 0.4429); and of the renal operations (solitary/ multiplex bone: p=0.0452; solitary/ multiplex extraosseal: p=0.0191; multiplex bone/ multiplex extraosseal: p=0.1125). However, the localization of the multiplex metastases (if they had an extraosseal (multiorganic) or bone only localization) did not influence the survival (Fig. 2a and b).

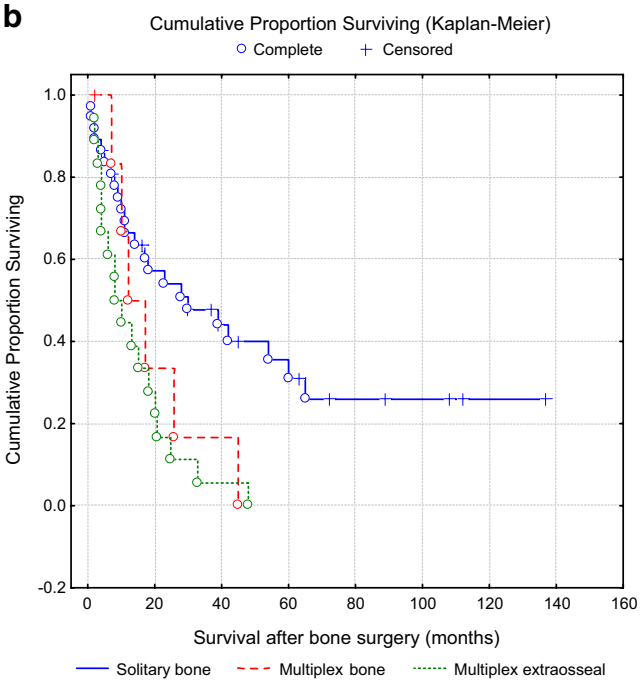
The Correlation Between the Localization of the Metastases in the Bone System and the Survival - Metastases were originated axially in 10 cases (15.4%), in the shoulder girdle, pelvis (vertebrae and sacrum were excluded), and in 55 cases (84.6%) they occurred in the limbs, especially in tubular bones, they involved a metacarpus and a talus in 1 case each. Accordingly, the localization in the bone system (axial or peripheral) did not show any correlation with the survival neither after renal (p=0.1787) nor after bone surgery (p=0.4786). Moreover, on the patients who underwent radical surgery for solitary bone metastasis, no connection between the localization and the survival was observed.

The Correlation Between the Radicality of Surgery and the Survival - Orthopedic interventions were categorised into the following groups: A: radical resection of solitary



(solitary/multiplex bone: p=0.0452; solitary bone/multiplex extraosseal: p=0.0191; multiplex bone/ multiplex extraosseal: p=0.1125)

Solitary bone: n=37
Multiplex bone: n=10
Multiplex extraosseal: n=18

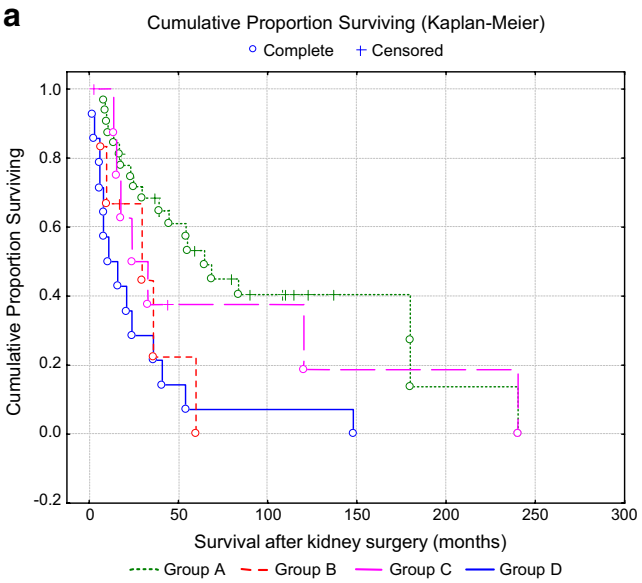


(solitary/ multiplex bone: p=0.1762; solitary bone/ multiplex extraosseal: p=0.0028; multiplex bone/ multiplex extraosseal: p=0.4429)

Solitary bone: n=37
Multiplex bone: n=10
Multiplex extraosseal: n=18

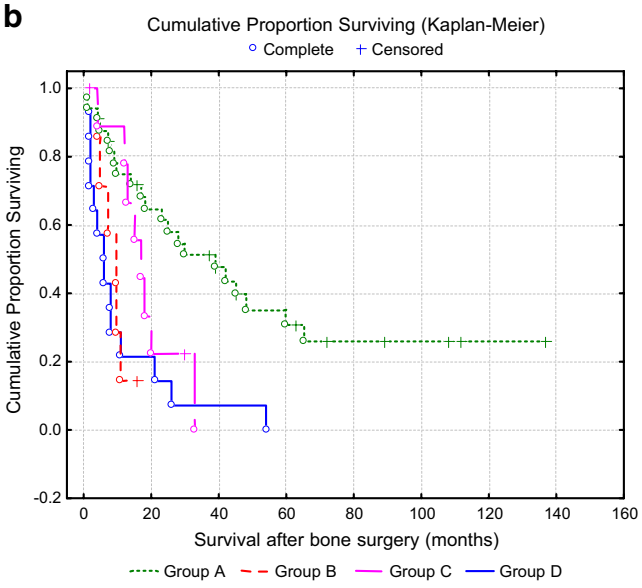
Fig. 2 **a**: Correlation between multiplicity of bone metastases and survival after kidney surgery. **b**: Correlation between multiplicity of bone metastases and survival after bone surgery

metastasis, B: intralesional removal of solitary metastasis, C: locally radical resection in the case of multiplex metastases, D: transfocal fixation or biopsy in the case of multiplex metastases, advanced disease. Significantly longer survival can be expected after radical bone surgery in the cases of solitary metastasis (group A), while in the other groups (B, C and D) there were no significant differences (Fig. 3b). The survival after the renal operation is better in group C of patients (who underwent radical surgery with further metastases), moreover, it shows similarity to the values in group A (Fig. 3a).



(D/A: p:0.0010; B/A: p=0.0275; C/A: p=0.4712; D/B: p=0.3134; D/C: p=0.0107; B/C: p=0.4003).

Radical surgery (A): n=33
Surgery with positive surgical margin (B): n=7
Radical surgery (locally)+distant metastasis (C): n=10
Biopsy, intralesional fixation (D): n=15

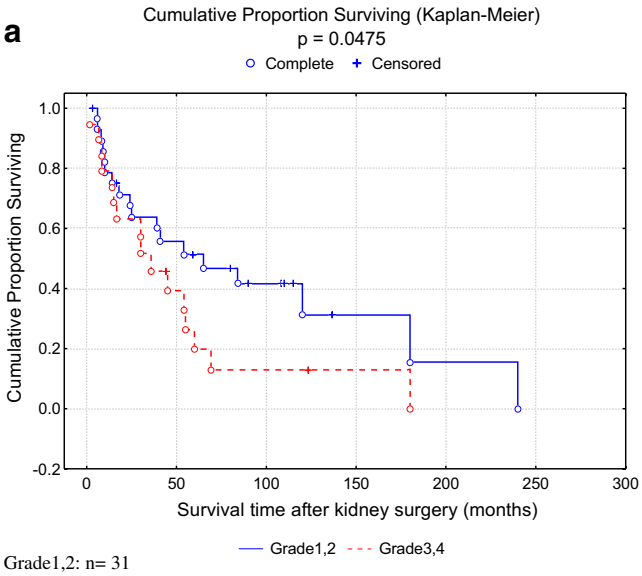


D/A: p:0.0017; B/A: p=0.0479; C/A: p=0.0459; D/B: p=0.3288; D/C: p=0.0251; B/C: p=0.0395

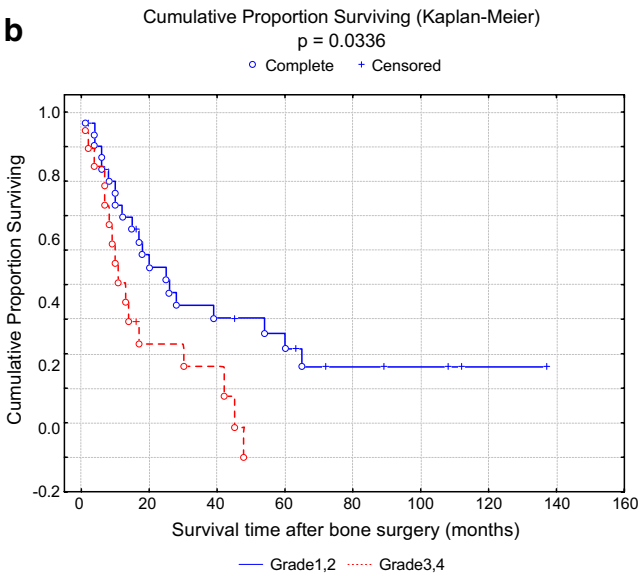
Radical surgery (A): n=33
Surgery with positive surgical margin (B): n=7
Radical surgery (locally)+distant metastasis (C): n=10
Biopsy, intralesional fixation (D): n=15

Fig. 3 **a**: Correlation between radicality of bone surgery and survival after kidney surgery. **b**: Correlation between radicality of bone surgery and survival after bone surgery

The Relation Among the Stage, Grade of Primary RCC and Survival - Primary RCC stemmed from both kidneys as



Grade1,2: n= 31
Grade3,4: n= 19



Grade1,2: n= 31
Grade3,4: n= 19

Fig. 4 **a**: Relationship between grades of bone metastases and patients survival after renal surgery. **b**: Relationship between grades of bone metastases and patients survival after bone surgery

origin, and the distribution of stages and the grades could be found in Table 1. As a consequence, we got the result that the stage and the grade of primary RCC did not influence survival after renal surgery (stage:1/2: p=0.2110; stage 1/3: p=0.7468; stage 2/3: p=0.1988); as well as after bone surgery (stage:1/2: p=0.0988; stage 1/3: p=0.6964; stage 2/3: p=0.1422).

The Correlation Between the Grade of Bone Metastasis and Survival - Significantly longer survival could be detected both after renal (p=0.0475) and bone surgery (p=0.0336) of patients with grade 1 and 2 bone metastases, than in the case of higher (3,4) grades. (Fig. 4a, b) Focusing on the changes of Fuhrman grade in the primary and metastatic lesions, the grade of the bone metastasis was lower than the grade of primary tumours in 29,5% of cases, the grade of metastasis was higher in 44,0%, and no change of grade was observed in 26,5% (Fig. 5).

Survival - Fifteen patients (23,0%) are still alive (average survival: 67.8 months (3–137) after renal and 51.8 (2–137) months after bone surgeries; and 50 patients died (77%, average survival: 47.1 months (2–240) after the renal and 17 months (1–65) after the bone operations. Table 2 shows the survival data with Life Table method.

Applying **Cox's regression** for the parameters of gender, age, symptoms, localisation of the bone metastases, their

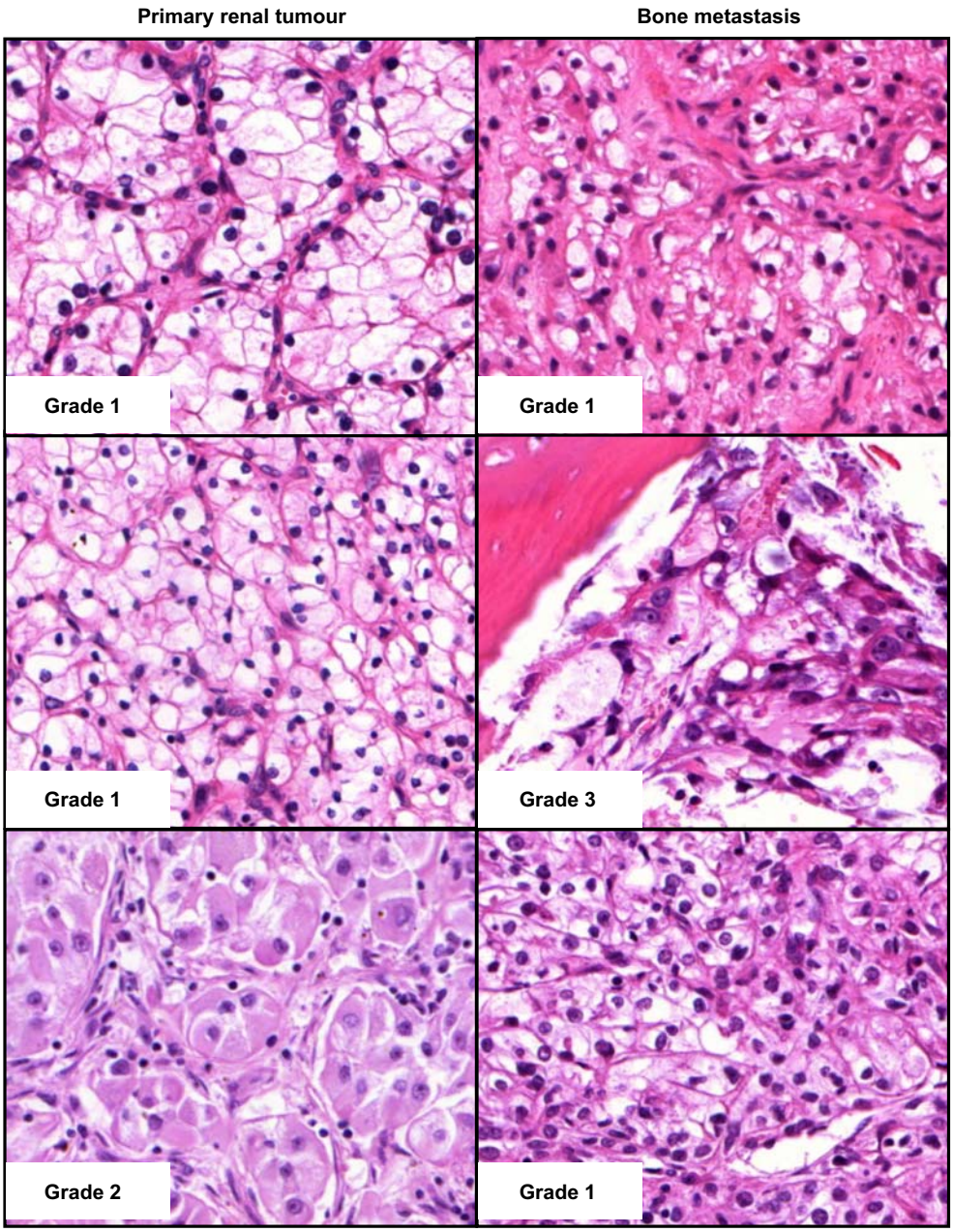


Fig. 5 Grade changes between the primary renal cell tumours and bone metastases

Table 2 Life table method: the percent values mean the cumulative proportion of surviving

Examined parameters	No of population at the beginning of follow up (N)	Follow up time after bone surgery (years)										
		1	2	3	4	5	6	7	8	9	10	11
Total study population	64	58.4%	39.5%	30.3%	24.0%	19.2%	14.1%	12.5%	10.7%	8.9%	6.7%	3.3%
Group A (radical surgery)	33	75.0%	61.6%	51.3%	39.9%	35.5%	26.0%	23.1%	19.8%	16.5%	12.4%	6.2%
Group B,C,D (all patients but group A)	31	40.9%	16.0%	6.8%	3.4%							
Solitary bone metastasis	38	67.5%	52.8%	46.4%	39.0%	34.6%	25.4%	22.6%	19.3%	16.1%	12.1%	6.0%
Multiplex bone metastases	24	48.9%	22.2%	8.9%	4.4%							
		Follow up time after kidney surgery (years)										
Total study population	61	78.5%	63.1%	52.6%	43.2%	36.9%	30.3%	29.2%	26.9%	25.7%	24.3%	21.1%
Group A (radical surgery)	32	87.5%	74.7%	68.2%	61.2%	53.3%	45.1%	43.0%	38.4%	36.0%	33.2%	29.6%
Group B,C,D (all patients but group A)	29	68.4%	49.9%	34.5%	22.3%	17.9%	13.4%	11.1%	9.3%	7.7%	6.4%	4.3%
Solitary bone metastasis	37	83.7%	69.8%	61.0%	57.8%	50.4%	42.6%	40.6%	36.3%	34.0%	31.4%	27.9%
Multiplex bone metastases	23	73.3%	55.0%	41.2%	22.9%	18.3%	13.7%	11.4%	9.5%	7.9%	6.6%	4.4%

size, Fuhrman grade, as well as multiplicity, date of recognition, pathological fracture, expansion into soft tissues, the radicality of surgery, the stage and grade of primary RCC, it was discovered, that the multiplicity, grade of metastases and the surgical radicality are the factors influencing survival after bone surgery (Table 3). Analysing the survival after renal operations, the multiplicity and grade of bone metastases and their detection date were the influencing factors of survival, independently from other parameters.

The differences among the patients, who survived more than 5 years after bone and renal operation and the others who died within 5 years were also investigated. In the cases of patients surviving the orthopedic operations by at least 5 years, the solitary, low grade (1,2) metastases were more featuring and more radical surgeries were performed in comparison to those, who died (Table 4). As we regard the date of the renal operation as the initial time, the grades of metastases were lower (1,2) and recognition was much later in the long survival group.

Discussion

The osteolytic bone metastases of RCC typically present symptoms, pain, pathological fracture and compression of

Table 3 Cox regression analysis

Variables	Relative Risk (RR) (after bone surgery)	p* (after bone surgery)	Relative Risk (RR) (after kidney surgery)	p* (after kidney surgery)
Gender	0.6274	0.2341	0.7921	0.5270
Age	1.0134	0.4098	1.010	0.5488
Onset time of bone metastases	1.0682	0.0915	0.7220	**<0.0005**
Symptoms	0.6810	0.5534	1.7465	0.4097
Pathological fracture	0.7261	0.4356	0.6697	0.2960
Size of bone tumour	1.0091	0.7584	0.9972	0.9393
Solitary/Multiplex	2.3490	**0.0223**	3.1677	**0.0014**
Localisation of bone metastases	1.0097	0.9841	1.3716	0.5350
Radicality of surgery (A,B,C,D)	0.6137	**0.0029**	0.7810	0.1155
Stage of primary kidney tumour	1.5647	0.1669	1.3211	0.4350
Grade of primary kidney tumour	1.0349	0.9022	1.2354	0.5108
Grade of bone metastases	3.2365	**0.0012**	3.3807	**0.0007**

*: Wald statistics

Table 4 Comparison of patients lost within 5 years after bone surgery and patients with longer survival

Variables	Survival after bone surgery	Survival after kidney surgery
Gender	0.8216	0.2364
Age	0.7996	0.7780
Onset time of bone metastases	0.7160	**0.0002**
Symptoms	0.2888	0.3431
Pathological fracture	0.4230	0.8086
Extracortical involvement	0.3170	0.5685
Size of bone tumour	0.9254	0.3288
Solitary/Multiplex	**0.0034**	0.1291
Localisation of bone metastases	0.7895	0.5326
Radicality of surgery (A,B,C,D)	**0.0086**	0.0781
Grade of primary kidney tumour	0.1327	0.2300
Grade of bone metastases	**0.0181**	**0.0233**

the spinal chord in their early stage. Their response rate of interferon alpha or interleukine-2 therapy is only 15–20%, and this has no effect on bone metastasis [8]. Therefore the patients often need palliative surgery, pain-killers or local irradiation. These therapies aim at pain relief, to prevent pathological fractures, to stabilize fractures or to provide the mobility for patients. The palliative therapy of metastases of RCC localized on the long tubular bones can be managed with minimal invasive surgical methods, however the tumour is not removed, so the life expectancy of patients is poor. The opportunity for radical surgery of solitary bone metastases is given only in limited cases [7]. On the one hand, radical excision of the metastasis with prosthesis replacement places higher burden on patients and it requires special surgical skills and objectives. On the other hand, it results in better life qualities. It is still questioned if radical excision influences the survival. Moreover, ambiguous data were found in the literature regarding the effects of pathological fracture and multiplicity on survival [6, 9]. There were no data found in the literature about the prognostic relevance of Fuhrman grade of the bone metastases. The pathological and clinical factors influencing prognosis are evaluated, hoping that these results will contribute to the management of patients with RCC bone metastases.

The age, gender of patients, symptoms caused by the metastases had no influence on the survival, regarding the date of both bone and renal operations with utilizing any of the methods (Kaplan-Meier, Cox regression), similarly to the data in the literature [4, 6, 8-12].

In certain cited cases, the survival of patients are calculated from the date of renal surgery. These references are pointing at better survival in the case of late metastases [13]. Our results confirm these data. The survival was not affected, whether the metastasis was diagnosed at the same time with the tumour (synchronous) or during the following 4 years (early metachrone metastasis); a longer survival was experienced only when the metastasis occurred more than 4 years after the surgery. The survival from the date of bone surgery was not influenced by the onset time of metastases. Significant survival difference was only experienced following the renal surgery of late onset metachrone metastasis group, and according to the definition of this group, the appearance of bone metastases was more than 4 years after surgery, and this time is calculated by the survival after renal surgery.

Pathological fracture and the spread of the tumour into soft tissue did not affect the survival in our material either concerning all of the cases or only regarding the patients with solitary metastasis. Literature data concerning these fields are very indefinite, some report the same results [10, 12], while others experienced worse survival in the case of pathological fractures [7].

According to our results and to the observations of Dürr, the localization of bone metastasis did not have any influence on survival after bone or renal surgery [12]. However, these facts have to be handled carefully as our population did not contain spinal metastases with the worst prognosis and surgically only palliative treated (decompression, stabilization), moreover the number of the occurrence in the plain bones of pelvis as well as shoulder girdle is negligible [10].

The size of bone metastasis had no influence on the survival of patients, either. There is, however, a relation between the size of primary RCC-s and their potency of giving metastasis and it is considered as a major prognostic factor. On the contrary, our results showed that if metastasis has already been triggered, the survival is affected not by the size of the metastasis, but by the multiplicity and by the surgical removability.

The type of surgery significantly influenced patients' survival after bone surgery. Should the radical removal of solitary metastasis have happened (group A), more essential survival data could be collected than in the cases, when known tumour remaining after orthopedic surgery (distant metastasis or locally intralesional therapies). The people in group C (who had local radical metastasectomy with the presence of distant metastasis in other localizations) survived five months longer than patients in group B (who had to their solitary bone metastasis local intralesional intervention). These previously mentioned facts could be proven by the acceleration of local growth and renewal due to surgical interventions. The shortest survival was experienced, as expected, when only transfocal fixation or biopsy were performed. Processing these results it should be noted, that the population was not randomized. When patients had poor conditions and their life expectancy was assumed to

be less than 3–6 months, only biopsies were performed. In the cases of solitary metastases and in a number of multiplex metastases, the lesions were radically removed. The multiplicity, the location, the pathological fractures (or the risk of them), the general condition, comorbidities and the age of patients altogether determined, whether the therapy was radical or palliative. Now it is really obvious that the differences in survival could be strongly influenced by these factors.

Contrary to Toyoda, Althausen, Han and Lin, there was no difference in the survival whether the multiple metastases proved to be multi organic or appeared in the skeletal system only [4, 8-10].

The Fuhrman system is the most widely used nuclear grading system for renal cell carcinoma [14, 15]. Although Fuhrman grade is widely accepted as a significant prognostic factor, its reproducibility and interobserver differences, as reported by Lang and Ficarra, appears to be moderate [14, 16, 17]. The substantial overlap in survival curves for grade 1 and grade 2; and for grade 3 and grade 4 tumours provided an opportunity to cluster those categories, and the resulting two-tiered nuclear grading system was an independent predictor of cause-specific survival in patients with renal cell cancer and simultaneously led to an improvement in interobserver agreement and reproducibility [16, 17]. According to Lin, the Fuhrman grade of the primary renal cell tumour was not predictive of long-term survival in case of bone metastases [9].

We studied the Fuhrman grade both in the primary and metastatic tumours, and their influence on patients survival. According to Poel, the stage and grade of primary tumours did not affect the survival of patients with bone metastasis [18].

Focusing on the changes of Fuhrman grade in the primary and metastatic lesions, the grade of the bone metastasis was lower than the grade of primary tumours in 29,5% of cases, the grade of metastasis was higher in 44,0%, and no change of grade was observed in 26,5%. Only one author, Onishi and co-workers investigated the grade changes between primary renal tumours and distant metastases. They concluded that over half of metastatic lesions did not coincide with the primary lesion [19]. He observed low grade metastases (1,2) in lung, spleen, adrenal gland and brain in 80%. On the other hand, as to the osseous metastasis, the rate of high grade malignancy (3,4) was 87.5%. We could not confirm their results, 62% of the bone metastases were low grade (1,2). However, to our knowledge, the prognostic significance of the Fuhrman grade of bone metastasis of renal cell carcinoma has not been previously analysed. In our survey the grade of bone metastasis influenced significantly the survival after renal or bone operations, in the cases of low grade (1,2) metastases can be expected longer survival, compared to patients with higher grades (3,4). Should the bone metastasis have recently been set, the behaviour of the disease and therefore the predestination of patients mostly depend on the grade of metastases. In renal cell cancer patients with bone metastases palliative, minimal invasive surgery should mostly be performed, while in the presence of positive prognostic factors radical surgery can be considered to achieve longer survival (35,5% at 5 years in our material) [20-22]. According to our results the Fuhrman grade of metastases should be taken into consideration at the indication for surgery of bone metastases.

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