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Prognostic factors of overall survival in renal cancer patients – single oncological center study

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INTRODUCTION

The clinical course of renal cancer remains difficult to predict. Attempts to appoint new independent prognostic factors (IPFs) and comparisons of already identified ones among populations are inevitable to develop more effective prognostic instruments. The aim of this study was to evaluate IPFs of overall survival in a given population of patients with renal cancer.

Materials and methods. Retrospective analysis of 148 patients with renal cancer treated at the Oncological Institute in Cracow from 2000 to 2007 was performed. Mean follow-up was 51 months. Using the log-rank test, a group of clinicopathological and biochemical features was analyzed in respect to their influence on overall survival. Results were presented as Kaplan–Meier curves. Final identification of IPFs was made by multivariate Cox regression analysis.

Results. Overall survival rate at 1, 2, and 5-year follow-up was 58.8%, 38.2%, and 21.4%, respectively. The set of identified IPFs consisted of performance status, smoking history, hemoglobin concentration, anatomical staging, tumor grade, and the presence of microvascular invasion. It was confirmed that only nephrectomy increases significantly overall survival.

Conclusions. Apart from smoking history, the role of all other IPFs identified in our study is well documented in the literature. Smoking history seems to be a new IPF with strong negative impact on survival in patients with RCC.

INTRODUCTION

The course of renal cancer is highly unpredictable. Patients with small tumor may have distant metastasis with adverse prognosis, while patients with metastasis to lymph nodes, after nephrectomy may live more than five years [1, 2].

In numerous studies over last decade, new clinicopathological features expected to support prognostication in various groups of patients with RCC (i.e. before or after treatment, with or without metastatic disease) were considered [3]. Among them some clinical (symptoms, performance status), histological (tumor subtype, histological grade, microvascular invasion), biochemical (hemoglobin, calcium concentrations, LD serum activity), molecular, and cytogenetic variables turned out to provide additional prognostic information, as they correlate with long term follow-up outcomes reported in previously performed studies [4, 5, 6]. Based on these data, and independent prognostic factors (IPFs), new scoring systems assessing the clinical course of renal cancer were proposed [7].

Among the variety of major scoring systems referring to renal cancer, it is remarkable how different sets of IPFs they may use, depending on aspects of
a prognosis they are about to assess and groups of patients they apply to. For instance Karakiewicz nomogram (KN) predicts 1-, 2-, 5-, and 10–year of cancer specific survival for the patients with renal cancer in all stages. This post–surgery nomogram uses as IPFs: TNM classification (2002), tumor size, tumor grade according to Fuhrman, histological tumor sub–type, patient’s age, and presence of symptoms [8]. Another scoring system, assessing overall survival of the patients with metastatic renal cancer disease was proposed by Motzer. The IPFs set according to this model included: Karnofsky perfor-

cance status, hemoglobin concentration, serum calcium concentration, serum lactate dehydrogenase activity (LDH), and time passed from diagnosis to treatment [9].

One of the merits of the current prognostic tools is the fact that their efficacy is measurable. It is expressed by prediction accuracy (PA), a value that falls within the range from 100% (an ideal confidence of the prediction) to 50% (what represents the outcome probability assessment equal to a toss of a coin) [3]. This allows to compare scoring systems to one another and to evaluate their prognostic efficacy for different populations (external validation). It is stressed in the literature that the discriminating ability of a particular scoring systems vary among populations, depending on ethnic dissimilarities and quality of treatment (diagnostic and therapeutic standards functioning in local healthcare system, i.e. methods of histopathological examination, agents available in adjuvant therapy) [10–14]. It is necessary to confirm the usefulness of the IPFs defined previously and prognostic tools in various populations of patients [3, 15].

MATERIAL AND METHOD

Retrospective analysis of 148 patients with renal cancer, treated at the Oncological Institute in Krakow in years 2000–2007, was performed. Mean age of the analyzed group of patients was 59.6 years (range: 33 to 79), mean observation time was 51 months (range 5 to 109 months). Staging (according to TNM scale, version for the year 2002) was estimated based on computer tomography with contrast and lung radiogram [16]. Basing on the same clinical data, the patients were divided according to anatomic stages (TNM grouping according to AJCC, 2010).

In case of suspicion of metastasis to bones or the central nervous system, additional imaging studies were performed. Kidney removal was performed according to standard criteria and was accompanied by local lymphadenectomy, if they were palpable during surgery or enlarged in imaging studies. After surgery, patients were followed up no less than every

| Variable                  | is | n   | %   |
|---------------------------|----|-----|-----|
| Sex                       |    |     |     |
| Male                      | 102|     | 68.9|
| Female                    | 46 |     | 31.1|
| Smoking history            |    |     |     |
| Yes                       | 103|     | 69.6|
| No                        | 45 |     | 30.4|
| Symptoms                  |    |     |     |
| Pain                      | 87 |     | 59.2|
| Haematuria                | 29 |     | 19.9|
| Tumour                    | 4  |     | 2.7 |
| Weakness                  | 8  |     | 5.4 |
| Loss of body weight       | 5  |     | 3.4 |
| No symptoms               | 33 |     | 22.3|
| Metastasis location       |    |     |     |
| Lungs                     | 52 |     | 35.1|
| Liver                     | 18 |     | 12.2|
| To bones                  | 52 |     | 35.1|
| To brain                  | 6  |     | 4.1 |
| To lymph nodes            | 80 |     | 51.4|
| Other                     | 8  |     | 5.4 |
| Feature T acc. to TNM v. 2002 | |     |     |
| T1                        | 17 |     | 14.3|
| T2                        | 29 |     | 24.4|
| T3a                       | 45 |     | 37.8|
| T3b                       | 22 |     | 18.5|
| T4                        | 6  |     | 5.0 |
| Feature N                 |    |     |     |
| N0                        | 18 |     | 18.4|
| N1                        | 80 |     | 81.6|
| Feature M                 |    |     |     |
| M0                        | 13 |     | 10.1|
| M1                        | 116|     | 89.9|
| Fuhrman grade             |    |     |     |
| I                         | 7  |     | 6.6 |
| II                        | 29 |     | 27.4|
| III                       | 52 |     | 49.0|
| IV                        | 18 |     | 17.0|
| Histological subtype      |    |     |     |
| Clear cellular            | 34 |     | 46.6|
| Papillary                 | 7  |     | 9.6 |
| Sarcomatoid               | 5  |     | 6.8 |
| Chromophobe               | 11 |     | 15.1|
| Collecting duct           | 1  |     | 1.4 |
| Unclassified              | 15 |     | 20.5|
| Microvascular invasion (MVI) | |     |     |
| No                        | 105|     | 70.9|
| Yes                       | 43 |     | 29.1|
| Nephrectomy               |    |     |     |
| No                        | 25 |     | 16.9|
| Yes                       | 123|     | 83.1|
| Chemotherapy              |    |     |     |
| No                        | 105|     | 70.9|
| Yes                       | 43 |     | 29.1|
| Immunotherapy             |    |     |     |
| No                        | 134|     | 90.5|
| Yes                       | 14 |     | 9.5 |
| Targeted therapy          |    |     |     |
| No                        | 132|     | 89.2|
| Yes                       | 16 |     | 10.8|
| Hormonotherapy            |    |     |     |
| No                        | 124|     | 83.8|
| Yes                       | 24 |     | 16.2|
| Radiotherapy              |    |     |     |
| Bones                     | 50 |     | 33.8|
| Lungs                     | 1  |     | 0.7 |
| Brain                     | 4  |     | 2.7 |
| Local recurrence          | 10 |     | 6.8 |
| Symptomatical treatment   |    |     |     |
| No                        | 98 |     | 66.2|
| Yes                       | 50 |     | 33.8|
six months. In the post–surgery surveillance, apart from history and physical examinations, blood analysis (morphology, biochemical analysis) and imaging studies (chest x–ray, abdominal cavity ultrasound and CT) were performed. In case of bone pain, either bone x–ray or scintigraphy was performed. In case of the lack of technical possibilities of surgical removal of kidney or due to the patients’ general state, they were qualified for immunotherapy or other types of treatment. The patient’s cause of death was designated based on death certificate, the leading urologist inscription, or interview with the family members.

Statistical analysis

Continuous quantitative variables were characterized using arithmetic mean, median, range, and standard deviation. Categorical variables were reported as proportions expressed in percentages. Patients were divided into cohorts in respect to each variable. The cumulative overall survival rates in subsequent years of follow–up were calculated for the entire group and for each cohort separately. In the same way, the Kaplan–Meier cumulative survival probability curves were plotted. In the univariate analysis, using log–rank test, differences in overall survival between cohorts and their statistical significances were assessed. Factors influencing overall survival were included in multivariate Cox regression analysis, which gave final identification of independent prognostic factors in the analyzed group of patients. Basic statistical significance level used in the paper was p <0.05. The characteristics of the analyzed group are presented in table 1.

RESULTS

The 1, 2, 3, 4, and 5–year cumulative survival probability in the entire group of patients was 58.8%, 38.2%, 32.7%, 29.1%, and 21.4%, respectively. Our study comprised patients with RCC in all stages. However, the majority of them (89.9%) were metastatic. Most of the patients in our group died due to the cancer, and cancer specific and overall survival did not significantly change in value. All clinicopathological and biochemical data were evaluated for their influence on overall survival (OS). There were no differences in survival rates in respect to sex (5–year survival: F–19.8%, M–27.1% p = 0.3068), whereas analysis of age distribution by the use “k–mean” method revealed two points of highest morbidity: 51.5 and 69 years. Results of univariate analysis describing the influence of each variable on overall survival in our group of patients were gathered in tables 2, 3, 4, and 5. Selected factors were also presented as Kaplan Meier curves.

Univariate analysis

Prognostic factors from history and physical examination (Table 2).

### Table 2. Overall survival rate [%] according to factors from history and physical examination

| Feature       | n  | Years of follow-up | Significance |
|---------------|----|--------------------|--------------|
|               |    | 1st    | 2nd    | 3rd    | 4th    | 5th    |          |
| ECOG Performance Status |    | 0  | 88.9 | 88.9 | 88.9 | 88.9  | 63.5 | p <0.001 |
|               |    | 1  | 64.4 | 39.6 | 32.4 | 29.9  | 20.2 |
|               |    | 2  | 26.1 | 8.7  | 8.7  | 4.3   | 4.3  |
|               |    | 3+4* | 0.0  | 0.0  | 0.0  | 0.0   | 0.0  |
| Lumbar Pain  |    | No | 70.0 | 51.2 | 45.9 | 42.3  | 29.2 |
|               |    | Yes| 50.6 | 28.7 | 24.1 | 20.5  | 16.5 |
|               |    | 115| 51.3 | 32.2 | 26.1 | 22.5  | 17.5 |
| Symptomatic Presence |    | Asymptomatic | 33 | 84.8 | 59.5 | 56.2  | 52.9  | 36.4  |
|               |    | 103| 65.0 | 46.5 | 39.6 | 35.5  | 27.9 |
| Cigarettes Smoking |    | No | 44.4 | 18.7 | 16.4 | 14.0  | 9.4   |
|               |    | 45 | 26.1 | 8.7  | 8.7  | 4.3   | 4.3  |

*Groups with 3 and 4 points of ECOG PS were combined due to small quantities
In this group of factors ECOG performance status most substantially influenced overall survival (Figure 1). Patients with no clinical symptoms at the moment of diagnosis had much better prognosis than those with symptoms (p <0.001). Among symptoms reported in patient history, only lumbar pain at side of the affected kidney significantly affected overall survival (p <0.01). Other symptoms: overall weakness (p = 0.1138), body weight loss (p = 0.0559), hematuria (p=0.5242), and palpable tumor (p = 0.1289) were not statistically significant. Smoking history was a negative predictor of overall survival in the investigated group (p <0.001).

Prognostic factors from imaging (Table 3)

Comparing survival rates in groups subdivided according to TNM features and AJCC tumor stages (2010) substantial differences in overall survival rates were found (p <0.001) (Figure 2). Tumor extent (T feature acc. to TNM) delineated on the base of CT scanning was the only data obtained from imaging examinations, affecting overall survival with lower statistical significance (p <0.03). Exact localization of distant metastasis did not differ the overall survival (lungs (p = 0.4955), liver (p = 0.0519), bones (p = 0.0559), central nervous system (p = 0.4035), and others (p = 0.2543)).

Table 3. Overall survival rate according to TNM features and AJCC anatomic stage

| Feature                  | n   | 1st Year | 2nd Year | 3rd Year | 4th Year | 5th Year | Significance |
|--------------------------|-----|----------|----------|----------|----------|----------|--------------|
| Feature T in TNM         |     |          |          |          |          |          | p = 0.0386   |
| T1                       | 17  | 88.2     | 52.9     | 47.1     | 47.1     | 32.2     |              |
| T2                       | 29  | 75.9     | 50.6     | 39.7     | 36.1     | 28.1     |              |
| T3a                      | 45  | 53.3     | 33.3     | 28.6     | 23.8     | 20.8     |              |
| T3b                      | 22  | 54.5     | 31.8     | 27.3     | 27.3     | 10.9     |              |
| T4                       | 6   | 16.7     | 16.7     | 16.7     | 16.7     | .         |              |
| Feature N in TNM         |     |          |          |          |          |          |              |
| N0                       | 18  | 83.3     | 71.4     | 65.5     | 65.5     | 58.9     | p <0.005     |
| N1                       | 80  | 52.5     | 23.8     | 18.9     | 16.1     | 9.2      |              |
| Feature M in TNM         |     |          |          |          |          |          |              |
| M0                       | 13  | 100      | 84.6     | 84.6     | 84.6     | 68.4     | p <0.005     |
| M1                       | 116 | 55.2     | 33.2     | 26.0     | 21.4     | 15.4     |              |
| AJCC Anatomic stage 2010 |     |          |          |          |          |          | p <0.001     |
| I                        | 18  | 94.7     | 78.9     | 68.4     | 68.4     | 45.6     |              |
| II                       | 19  | 83.3     | 71.8     | 65.8     | 59.8     | 52.4     |              |
| III                      | 20  | 60.0     | 35.0     | 30.0     | 30.0     | 12.0     |              |
| IV                       | 74  | 44.6     | 18.1     | 13.9     | 10.8     | 7.2      |              |
Prognostic factors from histological examination (Table 4)

Statistical analysis did not show influence of histological subtype of the tumor on overall survival in the examined group of patients (type clear–cellular \( p = 0.9026 \), papillary \( p = 0.4180 \), sarcomatoid \( p = 0.8634 \), chromophobe \( p = 0.9933 \), collecting duct \( p = 0.2933 \), and other \( p = 0.9846 \)). However, the correlation of Fuhrman grade and overall survival rate was statistically significant \( p < 0.002 \) (Figure 3). Statistical significance referring to microvascular invasion in blood vessels was also noticed \( p < 0.04 \).

| Feature                        | n     | 1st | 2nd | 3rd | 4th | 5th | Significance |
|--------------------------------|-------|-----|-----|-----|-----|-----|--------------|
|                                |       | 1st | 2nd | 3rd | 4th | 5th |              |
| 1+2*                           | 36    | 77.8| 57.6| 57.6| 51.9| 38.1| \( p = 0.0002 \) |
| Fuhrman grade                  |       |     |     |     |     |     |              |
| 1+2                           | 3     | 69.2| 36.5| 26.4| 24.2| 15.4|              |
| 4                             | 18    | 27.8| 11.1| 11.1| 11.1| 11.1|              |
| Microvascular invasion         |       |     |     |     |     |     |              |
| No                            | 105   | 61.0| 45.7| 38.9| 33.9| 25.3| \( p < 0.001 \) |
| Yes                           | 43    | 53.5| 19.5| 17.0| 17.0| 11.3|              |

*Groups 1 and 2 were combined due to small quantities

Prognostic factors of overall survival in relation to the applied treatment

Patients with advanced renal cancer at the moment of diagnosis should undergo nephrectomy only if technically possible. By analysis of the influence of surgery on overall survival, it was shown that the group of patients after surgery lives much longer, based on 5–year observations \( p < 0.002 \) (Table 5/ Figure 4). The influence of nonsurgical treatment of the patients with advanced renal cancer was also evaluated. In the period between 2000 and 2007, (if nephrectomy was not possible) supplementary or main treatment consisted of cytokines (immunotherapy) administration. Unfortunately, no prolongation of patients’ life as a result of immunotherapy was noted \( p = 0.85 \). Other alternative treatment methods (chemotherapy \( p = 0.2844 \), hormonotherapy \( 0.5914 \), radiotherapy (for all radiated organs \( p < 0.4 \), and symptomatic treatment \( p = 0.1041 \)) also have no significant influence on overall survival.

| Nephrectomy performed: | n  | 1 year | 2 years | 3 years | 4 years | 5 years |
|------------------------|----|--------|---------|---------|---------|---------|
| No                     | 25 | 16.0   | 12.0    | 12.0    | 6.0     | 0.0     |
| Yes                    | 123| 67.5   | 43.5    | 36.8    | 33.5    | 25.3    |

**Table 5. Overall survival rate according to nephrectomy**

**Figure 3. Kaplan-Meier overall survivorship curves according to Fuhrman grade \( p = 0.0002 \).**

**Figure 4. Kaplan-Meier overall survivorship curves according to nephrectomy.**
Multivariate Cox regression analysis

The group of clinical, histopathological and biochemical data mentioned above were analyzed using multivariate Cox regression model with the aim of distinguishing independent factors of the overall survival prediction in a given population of patients with renal cancer. This analysis showed independent prognostic value of each particular factor in overall survival assessment and their usefulness. In the univariate analysis performance status expressed in Karnofsky scale and gammaglutamylotranspeptidase activity (GGTP) also appeared to have prognostic value; providing, however, that other variables were constant (Table 6).

Multivariate Cox model analysis revealed that several previously described factors had a statistically significant, independent influence on overall survival. The set of identified independent prognostic factors (IPFs) of overall survival (at p < 0.05) consisted of performance status, smoking history, hemoglobin concentration, AJCC anatomical staging, tumor grade, and presence of microvascular invasion. Presented data confirmed substantially longer survival rates of patients after surgery and indicated that nephrectomy is also an independent prognostic factor (p < 0.02) (Table 7).

DISCUSSION

Performance status (PS) had the strongest influence on OS in our case series, HR in group of patients with 2 and with 4 or 5 points of ECOG score was 2.78 and 14.92, respectively. This indexed measure of patient’s general health was primarily devised to help oncologists qualify patents to systemic treatment with respect to their ability to withstand its adverse effects. It was included in RCC prognostication for the first time by Elson in 1988. He used PS (expressed in ECOG scale) as an IPF of OS in metastatic patients who underwent chemotherapy [17]. In RCC prognostication, PS played a greater role as prognostic factor of OS in patients with metastatic disease, especially qualified to various immune or targeted therapies (majority of scoring systems predicting outcomes in these groups of patients included PS in their sets of IPFs (Motzer, Lebovich, Denskov, Manola, etc.) [9, 15, 18, 19] Among major prognostic tools designed for the general population of patients with RCC, only Zisman’s model focused on OS and identified PS as a prognostically useful variable [20, 21].

In the epidemiology of renal cancer, smoking is a well–documented risk factor of morbidity [22]. It is also an IPF of CCS in several other cancers, i.e. colon, bladder [23, 24]. However, information regarding its influence on survival in RCC is poor. Recently, researchers from UCLA published an extensive work describing the negative impact of smoking on clinicopathological features and survival outcomes in an investigated group of 802 patients with RCC [25]. There was a significant difference in distribution of adverse clinicopathological features (ECOG PS, severity of comorbidities, tumor extent, vascular invasion) with higher incidence in the smoking group. The analysis also showed the correlation between smoking history and frequency of p53 suppressor gene mutation, and confirmed p53 overexpression to be IPF of CCS in all patients. Multivariate analysis revealed smoking history to be IPF, both of CCS and OS in localized RCC, however, these results were not confirmed in the group of patients with metastatic disease. In our study, smoking history was an IPF of OS with HR ratio 3.27.

Serum hemoglobin was also found be an IPF of OS in our group. Anemia is a common finding in patients with cancer disease. In 2001 Caro et al. published a systemic quantitative review of 60 studies describing the role of anemia in various types of neoplasms [26]. In this review about 33% of patients were anemic and their median survival was decreased by 20–43%. Statistical analysis revealed a low hemoglobin level to be a negative predictor of OS, and the highest HRs were observed in cases of multiple myeloma and lymphoma (4.47 and 3.74, respectively). In anemic patients with RCC, HR was 1.9. The authors also highlighted controversies about the hemoglobin

| Table 6. Characteristics of continuous variables and univariate associations with survival |
|-------------------------------------|------|--------|--------|--------|
| Variable                          | n   | (RR)   | (CI)   | p value |
|-------------------------------------|------|--------|--------|--------|
| Age                                | 145  | 1.007  | 0.991–1.023 | 0.4127 |
| Tumor size on CT scans             | 102  | 1.013  | 1.005–1.021 | 0.0011 |
| Hb                                 | 104  | 0.883  | 0.810–0.962 | 0.0046 |
| RBC                                | 93   | 0.935  | 0.728–1.200 | 0.5982 |
| AP                                 | 63   | 1.001  | 0.999–1.004 | 0.3212 |
| Serum urea                         | 81   | 1.031  | 0.957–1.111 | 0.4196 |
| Serum creatinine                   | 80   | 0.997  | 0.989–1.003 | 0.3665 |
| WBC                                | 12   | 1.002  | 0.997–1.007 | 0.4473 |
| LD                                 | 36   | 0.999  | 0.997–1.001 | 0.3956 |
| GGT                                | 40   | 1.002  | 1.000–1.004 | 0.0188 |
| PLT                                | 15   | 1.002  | 0.999–1.006 | 0.1226 |
| Lung metastasis size               | 25   | 0.992  | 0.971–1.012 | 0.4294 |
| Liver metastasis size              | 15   | 0.998  | 0.971–1.026 | 0.9095 |
| Bone metastasis size               | 9    | 0.985  | 0.963–1.008 | 0.2016 |
| Lymph nodes metastasis size        | 15   | 1.003  | 0.981–1.025 | 0.8171 |
| Karnofsky PS                       | 141  | 0.711  | 0.611–0.828 | <0.005 |
level cut–off value, which ranged from 8.5 g/dl to 14 g/dl, and the unclear link between anemia and tumor progression (apart from malignancies affecting bone marrow and other reticuloendothelial sites). In renal cancer, anemia is considered to result from elevated levels of inflammatory cytokines and increased catabolism induced by the tumor. However, in metastatic patients it may also be caused by systemic therapies administered to them. Some prognostic models stratifying risk in metastatic patients qualified to immune or targeted therapies use a low hemoglobin level as a negative predictor (Motzer, Negrier, Manola) [19, 27, 28].

In renal cancer, as well as in most of neoplasms, tumor involvement is the basic and most crucial prognostic factor predicting the course of disease. The first formal scale assessing the anatomical advancement of renal cancer correlating with OS was proposed by Robson. In 1978, however, it was replaced by the TNM classification involving consensus of US experts associated with the Union Against Cancer and the American Joint Committee. AJCC anatomic stages categorize patients with particular constellations of TNM features in respect to substantial interferences with distant outcomes, which can also vary depending on clinical situation [2, 29]. For instance, 5–year cancer–specific survival in patients who underwent surgical procedure range from 90–95% for stage I, 75–85% for stage II, 60–70% for stage III, and 20–30% for stage IV [30, 31]. Overall survival regardless of intervention, estimated in over 3,700,000 cancer cases was recorded in the National Cancer Data Base (NCDB) as 84.7%, 82.9%, 59.8%, and 11.1% for 1st, 2nd, 3rd, and 4th stages, respectively (Analysis from year 2000) [32, 33]. These data show that the presence of systemic metastases results in the highest reduction in survival rates. Nodal involvement is also associated with substantial decrease in survival. Surgical treatment significantly increases overall survival regardless of disease advancement. These finding correspond with our results.

Tumor grade, next to TNM, is an approved independent prognostic factor included in several major nomograms (Frank, Karakiewicz, Zissmann) [16, 20, 31, 34]. Similar results were observed in our group. Another histological finding affecting RCC prognosis is presence of microvascular invasion. Klatte et al., analyzing cancer specific survival in 258 patients with papillary renal cancer confirmed the usefulness of this prognostic factor, and the nomogram he proposed is one of the highest prediction accuracy (94%) [35]. In our work, 2–and 5–year patients’ overall survival, in dependence to the presence of MVI, was

| Characteristic | n     | RR   | 95% CI         | p    |
|---------------|-------|------|----------------|------|
| Cigarettes smoking |       |      |                |      |
| no            | 103   | 1.000|                 |      |
| yes           | 45    | 3.275| 2.101–4.946    | 0.0000|
| ECOG Performance status |       |      |                |      |
| 0+1           | 96    | 1.000|                 |      |
| 2             | 23    | 2.781| 1.583–4.884    | 0.0004|
| 3+4           | 9     | 14.972| 5.781–38.775  | 0.0000|
| Haemoglobin concentration (continuous variable in g/l) | 114 | 0.888| 0.804–0.980    | 0.0185|
| Tumor diameter (continuous variable in cm) | 102 | 1.012| 1.004–1.021    | 0.0054|
| AJCC anatomic stage |       |      |                |      |
| I+II          | 37    | 1.000|                 |      |
| III           | 20    | 2.109| 1.064–4.183    | 0.0326|
| IV            | 74    | 3.286| 1.878–5.750    | 0.0000|
| Fuhrman grade |       |      |                |      |
| 1+2           | 36    | 1.000|                 |      |
| 3             | 52    | 1.762| 1.059–2.934    | 0.0293|
| 4             | 18    | 3.023| 1.519–6.016    | 0.0016|
| Microvascular invasion (MVI) |       |      |                |      |
| No            | 105   | 1.000|                 |      |
| Yes           | 43    | 1.628| 1.049–2.525    | 0.0296|
| Nephrectomy   |       |      |                |      |
| No            | 25    | 1.932| 1.100–3.394    | 0.0220|
| Yes           | 123   | 1.000|                 |      |
45% and 25% (p <0.05), respectively. While congruent results were reported by Lang and co–authors (71% and 62% respectively) [36].

CONCLUSIONS

Data regarding RCC prognostication in Polish literature are extremely poor. There are only a few Polish studies assessing RCC prognostic factors by the use of modern statistical tools like multivariate Cox regression analysis. The prognostic value of clinical variables (expressed as HR) varies in different studies even when they applied to similar group of patients. Their role is well established for some, but for others (hemoglobin concentration, smoking history) is still debatable. Smoking history seems to be new IPF with strong negative impact on survival in patients with RCC.

Present reviews of major scoring systems emphasize the difference of their discriminating ability in different populations. For instance, discriminating ability of postoperative nomogram designed by Karakiewicz for all stages RCC in external validation performed on Canadian and North American populations ranged between 84 and 88%. Yet, when tested on British population its value was 74% [3, 37].

None of the scoring systems have been validated for the Polish population. Polish clinicians just have to assume that foreign prognostic models are applicable to assess outcomes in their patients. This lack of certainty, apart from doubts in their additional value, is one of reasons discouraging clinicians from using scoring systems in RCC prognostication in Poland. We believe that Polish population deserves adequate validations of modern prognostic models and evaluation of IPFs of RCC progression.

References

1. Lughezzani G, Jeldres C, Isbarn H, Perrotte P, Shariat SF, Sun M, et al. Tumor size is a determinant of the rate of stage T1 renal cell cancer synchronous metastasis. J Urol. 2009; 182: 1287–1293.

2. Gospodarowicz MK, Miller D, Groome PA, Greene FL, Logan PA, Sobin LH. The process for continuous improvement of the TNM classification. Cancer 2004; 100: 1–5.

3. Meskawi M, Sun M, Trinh QD, Bianchi M, Hanssen J, Tian Z, et al. A review of integrated staging systems for renal cell carcinoma. Eur Urol. 2012; 62: 303–314.

4. Klatte T, Rao PN, de Martino M, LaRochelle J, Shuch B, Zomorodian N, et al. Cytogenetic profile predicts prognosis of patients with clear cell renal cell carcinoma. J Clin Oncol. 2009; 27: 746–753.

5. Ficarra V, Brunelli M, Cheng L, Kirkali Z, Lopez–Beltran A, Martignoni G, et al. Prognostic and therapeutic impact of the histopathologic definition of parenchymal epithelial renal tumors. Eur Urol. 2010; 58: 655–668.

6. Sun M, Shariat SF, Cheng C, Ficarra V, Murai M, Oudard S, Pantuck AJ, et al. Prognostic factors and predictive models in renal cell carcinoma: a contemporary review. Eur Urol. 2011; 60: 644–661.

7. Lane BR, Kattan MW. Prognostic models and algorithms in renal cell carcinoma. Urol Clin North Am. 2008; 35: 613–625.

8. Karakiewicz PI, Briganti A, Chun FK, Trinh QD, Perrotte P, Ficarra V, et al. Multi–institutional validation of a new renal cancer—specific survival nomogram. J Clin Oncol. 2007; 25: 1316–1322.

9. Motzer RJ, Mazumdar M, Back J, Berg W, Amsterdam A, Ferrara J. Survival and prognostic stratification of 670 patients with advanced renal cell carcinoma. J Clin Oncol. 1999; 17: 2530–2540.

10. Liu Z, Lv J, Ding K, Fu Q, Cao Q, Wang F. Validation of the current prognostic models for nonmetastatic renal cell carcinoma after nephrectomy in Chinese population: a 15–year single center experience. Int J Urol. 2009; 16: 268–273.

11. Cindolo L, Patard JJ, Chiodini P, Schips L, Ficarra V, Tostain J, et al. Comparison of predictive accuracy of four prognostic models for nonmetastatic renal cell carcinoma after nephrectomy: a multicenter European study. Cancer. 2005; 104: 1362–1371.

12. Tan MH, Li H, Choong CV, Chia KS, Toh CK, Tang T, et al. The Karakiewicz nomogram is the most useful clinical predictor for survival outcomes in patients with localized renal cell carcinoma. Cancer. 2011; 117: 5314–5324.

13. Hupertan V, Roupert M, Poisson JF, Chretien Y, Dufour B, Thiounn N, Mejean A. Low predictive accuracy of the Kattan postoperative nomogram for renal cell carcinoma recurrence in a population of French patients. Cancer. 2006; 107: 2604–2608.

14. Utsumi T, Ueda T, Fukasawa S, Komaru A, Suzuka T, Kawamura K, et al. Prognostic models for renal cell carcinoma recurrence: external validation in a Japanese population. Int J Urol. 2011; 18: 667–671.

15. Motzer RJ, Back J, Schwarz L, Reuter V, Russo P, Marion S, Mazumdar M. Prognostic factors for survival in previous treated patients with metastatic renal cell carcinoma. J Clin Oncol. 2004; 22: 3; 454–463.

16. The Karakiewicz nomogram is the most useful clinical predictor for survival outcomes in patients with localized renal cell carcinoma. Cancer. 2011; 117: 5314–5324.

17. Elson PJ, Witte RS, Trump DL. Prognostic factors for survival in patients with recurrent or metastatic renal cell carcinoma. Cancer Res. 1988; 48: 7310–7313.

18. Leibovich BC, Blute ML, Cheville JC, Lohse CM, Frank I, Kwon ED, et al. Prediction of progression after radical nephrectomy for patients with clear cell renal cell carcinoma: a stratification tool for prospective clinical trials. Cancer. 2003; 97: 1663–1671.

19. Manola J, Royston P, Elson P, McCormick JB, Mazumdar M, Négrier S, et al. Prognostic model for survival in patients with metastatic renal cell carcinoma: results from the international kidney cancer working group. Clin Cancer Res. 2011; 17: 5443–5450.

20. Zisman A, Pantuck AJ, Wieder J, Chao DH, Dorey F, Said JW, et al. Risk group assessment and clinical outcome algorithm to
predict the natural history of patients with surgically resected renal cell carcinoma. J Clin Oncol. 2002; 20: 4559–4566.

21. Zisman A, Pantuck AJ, Dorey F, Said JW, Shvarts O, Quintana D, et al. Improved prognostication of renal cell carcinoma using an integrated staging system. J Clin Oncol. 2001; 19: 1649–1657.

22. Ljungberg B, Campbell SC, Choi HY, Jacqmin D, Lee JE, Weikert S, Kiemeney LA. The epidemiology of renal cell carcinoma. Eur Urol. 2011; 60: 615–621.

23. Batty GD, Kivimaki M, Gray L, Smith GD, Marmot MG, Shipley MJ. Cigarette smoking and site-specific cancer mortality: testing uncertain associations using extended follow-up of the original Whitehall study. Ann Oncol. 2008; 19: 996–1002.

24. Fleshner N, Garland J, Moadel A, Herr H, Ostroff J, Trambert R, O’Sullivan M, Russo P. Influence of smoking status on the disease-related outcomes of patients with tobacco-associated superficial transitional. Cancer. 1999; 86: 2337–2345.

25. Kroeger N, Klatte T, Birkhäuser FD, Rampersaud EN, Seligson DB, Zomorodian N, et al. Smoking negatively impacts renal cell carcinoma overall and cancer-specific survival. Cancer. 2012; 118: 1795–802.

26. Caro JJ, Salas M, Ward A, Goss G. Anemia as an independent prognostic factor for survival in patients with cancer: a systemic, quantitative review. Cancer. 2001; 91: 14–21.

27. Motzer RJ, Bacik J, Murphy BA, Russo P, Mazumdar M. Interferon-α as a comparative treatment for clinical trials of new therapies against advanced renal cell carcinoma. J Clin Oncol. 2002; 20: 289–296.

28. Negrier S, Escudier B, Gomez F, Douillard JY, Ravaud A, Chevreau C, et al. Prognostic factors of survival and rapid progression in 782 patients with metastatic renal carcinomas treated by cytokines: a report from the Groupe Francais d’Immunotherapie. Ann Oncol. 2002; 13: 1460–1468.

29. Harmer MH. TNM classification of malignant tumours. Ed. 3. Geneva, Switzerland: Union International Contre le Cancer; 1978, p. 152.

30. Gettman MT, Blute ML. Update on pathologic staging of renal cell carcinoma. Urology. 2002; 60: 209–217.

31. Tsui KH, Shvarts O, Smith RB, Figlin RA, deKernion JB, Belldegrun A. Prognostic indicators for renal cell carcinoma: a multivariate analysis of 643 patients using the revised1997 TNM staging criteria. J Urol. 2000; 163: 1090–1095.

32. Marshall FF, Stewart AK, Menck HR. The National Cancer Data Base Report on Kidney Cancer. Cancer. 1997; 80: 2167–2174.

33. Kane CJ, Mallin K, Ritchey J, Cooperberg MR, Carroll PR. Renal Cell Cancer Stage Migration: Analysis of the National Cancer Data Base. Cancer. 2008; 113: 78–83.

34. Frank I, Blute ML, Cheville JC, et al. An outcome prediction model for patients with clear cell renal cell carcinoma treated with radical nephrectomy based on tumor stage, size, grade and necrosis: the SSIGN score. J Urol. 2002; 168: 2395–400.

35. Klatte T, Remzi M, Zigeuner RE, Mannweiler S, Said JW, Kabbnavar FF, et al. Development and external validation of a nomogram predicting disease specific survival after nephrectomy for papillary renal cell carcinoma. J Urol. 2010; 184: 53–58.

36. Lang H, Lindner V, Laturneux H, Martin M, Saussine C, Jacqmin D. Prognostic value of microscopic venous invasion in renal cell carcinoma. Long term follow up. Eur Urol. 2004; 46: 279–914.

37. Gontero P, Sun M, Antonelli A, Bertini R, Carini M, Carmignani G, et al. External validation of the preoperative Karakiewicz nomogram in a large multicenter series of patients with renal cell carcinoma. World J Urol. 2012; 31 July [Epub ahead of print].