Retrospective Epidemiological Study and Prognostic Factors of Renal Cell Carcinoma

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Abstract:

Background: Renal cell carcinoma (RCC) is the most common malignancy of the kidney in adults, accounting for 85% of renal tumors. The five-year survival rate of patients with renal cancer had been doubled over the last 60 years. The chance of survival is improved with early diagnosis. We aimed to evaluate the prognostic significance of demographic, clinical, anatomical, and histopathological prognostic factors for RCC.

Methods: A total of 131 patients with RCC who attended to Clinical Oncology and Nuclear Medicine Department, Mansoura University in the period from 1st January 2010 to 31th December 2020 were evaluated retrospectively. Patient and tumor characteristics were documented. All the factors were correlated with overall survival (OS) to evaluate their prognostic significance.

Results: The median OS was 24 months. The 2, 5, and 10-year OS were 50%, 26%, and 11% respectively. In univariate analysis of OS, age, performance status (PS), presence of hematuria, hemoglobin (Hg) level, neutrophilic count, lactate dehydrogenase (LDH) level, T stage, regional lymph node (LN) or distant metastasis, TNM stage, pathological type, tumor grade, and presence of rhabdoid and /or sarcomatoid features were statistically significant. In multivariate analysis age, PS, Hg level, pathological type, tumor grade, presence of rhabdoid and /or sarcomatoid features were independent prognostic factors.

Conclusion: Our study proved the value of demographic, clinical, anatomical, and histological prognostic factors for RCC. However, there were limitations in our retrospective study. Further prospective studies with large sample size are encouraged and molecular factors should be studied to improve predictive prognostic value.

Key words: Renal cell carcinoma, prognostic factors, overall survival

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Introduction:

Renal cell carcinoma (RCC) is the most common malignant tumor of the kidney in adults, accounting for almost 85% of all renal tumors [1]. Incidence is approximately around 11.3/100 .000 in several Eastern, Northern, European countries and North America to 1/100 .000 in African countries. Incidence rates of RCC for women are half of those for men. Recently, incidence rates are increasing in many countries, most evident in Latin America [2]. In Egypt, the Middle East Cancer Consortium reported incidence rates of 3.0/100,000 in men and 1.7/100,000 in women. However, these data are based on the Gharbiah Cancer Registry that covers only 3.4 million people from a total Egyptian population of 85 million [3]. Several papers have commented on the apparent lower incidence of RCC in Africa and Middle East compared to Europe and North America and contributing that to under-diagnosis and under-reporting [1]

Cigarette smoking, obesity, hypertension and acquired cystic kidney disease (ACKD) are the most known risk factors for sporadic RCC [4].

Patients were diagnosed with RCC presented with flank pain, gross hematuria, or a palpable abdominal

mass. Nowadays, most cases are diagnosed incidentally. This shift is related to the widespread of using non-invasive radiological techniques that performed for another reasons [5].

Renal cell carcinoma is recognized as a family of cancers derived from renal tubular epithelium, results from different genetic abnormalities with unique morphologic features [6]. Recently, the histological classification of RCC had changed obviously to be not a single entity but variable tumor subtypes based on either specific pathological or molecular features. It is divided into two large groups include clear cell RCC (ccRCC) and non-ccRCC [7].

Prognostic factors are sub-classified into clinical, anatomical, histological, and molecular factors. In general, the use of clinical, anatomical, and histological prognostic factors are supported by a higher level of evidence than molecular prognostic factors [6].

Treatment for RCC cases without distant metastasis is surgical nephrectomy either partial or total with or without lymph node (LN) dissection, the role of adjuvant treatment has not been established and remains under clinical trials [8]. The treatment of metastatic cases involves a complex interplay between systemic therapy and surgical management [9]. In the last years systemic treatment for metastatic cases had changed dramatically from a non-specific immune approach, to targeted therapy including vascular endothelial growth factor (VEGF) inhibitors, mammalian target of rapamycin (m-tor) pathway inhibitors, and to novel immunotherapy agents [10].

The 5-year survival rate of patients with kidney cancer had been doubled over the last 60 years. The chance of survival is improved with early diagnosis. The 5-year relative survival rate is 92% for localized tumors, 65% for tumors with regional lymph nodes metastasis, and 12% for distant metastasized tumors [11].

In our study we aimed to analyze the data of RCC patients who attended to Clinical Oncology and Nuclear Medicine Department, Mansoura University Hospital to define the prognostic factors and assess survival of the patients.

Patients and Methods:

The current study is a retrospective study of patients with RCC attended to Clinical Oncology and Nuclear Medicine Department in the period from 1st of January 2010 to 31st of December 2020 inclusive. Our study was submitted for approval by Institutional Research Board, faculty of Medicine, Mansoura University.

Inclusion criteria included pathologically confirmed RCC patients who were more than 18 years old. Patients with double malignancy were excluded from the study.

The registered patient characteristics were age, sex, smoking, medical history, family history, presenting symptoms including hematuria, loin pain, constitutional symptoms, and symptoms related to metastasis. Clinical examination was also recorded including body mass index (BMI), and performance status (PS) according to Eastern Cooperative Oncology Group (ECOG) scale. Laboratory tests included hemoglobin (Hg), neutrophil, platelets, albumin, and creatinine levels. Lactate dehydrogenase (LDH) and serum calcium levels were also documented if reported.

Regarding tumor characteristics, primary tumor side, size, and number of renal lesions, tumor extent, regional lymph node (LN), distant metastasis, and TNM staging were recorded. The pathological type, grading and presence of lymphovascular emboli (LVE), rhabdoid and/or sarcomatoid features was also documented

The end point of our work is to study RCC patients and asses demographic, clinical, anatomical, and histological prognostic factors affecting OS that was calculated from date of diagnosis to date of death, loss follow up, or the end of the study.

Statistical Analysis

The available data were coded, tabulated and analyzed. IBM SPSS software package version 26 for Windows (Statistical Package for Social Sciences) was used. The appropriate statistical tests were used. Qualitative data were presented as numbers and percent. Quantitative data was presented with median and range. OS was analyzed using Kaplan Meier survival curves and comparison was done by log rank test. Cox proportional hazards models used to calculate the univariate and multivariate analyses for prognostic factors which affected the survival. The level of significance was considered at 5%, the differences were considered statistically significant for the analysis when p was ≤ 0.05.

Results:

In our retrospective study 134 patients attended to our department in the study period. They were confirmed radiologically and pathologically to have RCC. Three cases were excluded in view of having double malignancy.

The patient characteristics were summarized in table (1). The median age of patients was 56 years with range of (19-78 years). Male predominance was observed with male to female ratio1.6:1. The majority of patients were non-smoker (78.6%). About 58.8% of cases had associated comorbidities of which hypertension (HTN), hepatitis C virus (HCV) infection, diabetes mellitus (DM), and associated renal diseases were the commonest. The family history was nearly 10% of cases. Most of patients (69.5%) presented with ECOG PS ≤ 1. One hundred and fifteen of the studied cases were symptomatic (87.8%). Loin pain and hematuria were the most frequent symptoms. In present study anemia was presented in 45% of cases. Neutrophilia and thrombocytosis were presented in 6.1% and 4.6 % respectively. In current analysis, most of cases had normal albumin and creatinine levels. Lactate dehydrogenase and calcium levels were not recorded in most cases.

We summarized tumor characteristics in table (2). The bilateral, multicentric or multifocal lesions were

reported in 0.8% and 3.8% respectively. Seventy-eight cases presented with tumor size ≤ 10 cm (59.5%). Early T Stages (T1 and T2) were presented in 26.0% and 42.0% respectively. Regional LN metastasis was found in 46 cases (35.1%) and 61 cases (46.6%) had distant metastasis at diagnosis. Stage IV was diagnosed in 62 cases (47.3%). Clear cell RCC was reported in 57.3 % while papillary RCC (pRCC) in 16.8 % of cases. Grade II and III were the most frequented reported grades that were presented in 28.2% and 23.7% respectively. Lymphovascular emboli, rhabdoid and /or sarcomatoid features were reported in 3.1% and 13.7% respectively.

Regarding the OS; the median OS for patients was 24 months (CI 16.61-31.39). The 2, 5 and 10-year OS were 50%, 26%, and 11% respectively (figure 1).

The prognostic factors affecting OS were mentioned in table (3). Starting with univariate analysis; factors that were associated with worse prognosis with a statistically significant correlation with OS were increasing age (P: 0.027), presence of neutrophilia (P: 0.013), LDH level > 1.5 upper limit of laboratory reference range (ULLRR) (P: 0.025), advanced T stages (P: 0.001), non- ccRCC or mixed tumors (P: 0.010), presence of rhabdoid and / or sarcomatoid features (P: 0.001). Also, poor EGOG PS, presence of anemia, regional LN or distant metastasis, advanced TNM stages, and high tumor grades had a highly significant negative correlation with OS (P <0.001). On the other hand, the presence of hematuria was associated with improvement of OS with a significant prognostic value (P :0.032). In multivariate analysis significant independent prognostic factors for OS were age (P:0.001), ECOG PS (P:0.001), presence of anemia (P:0.004), presence of rhabdoid and /or sarcomatoid features (P:0.020). Pathological type and tumor grade were also independent prognostic factors with a highly significant statistically correlation (P <0.001).

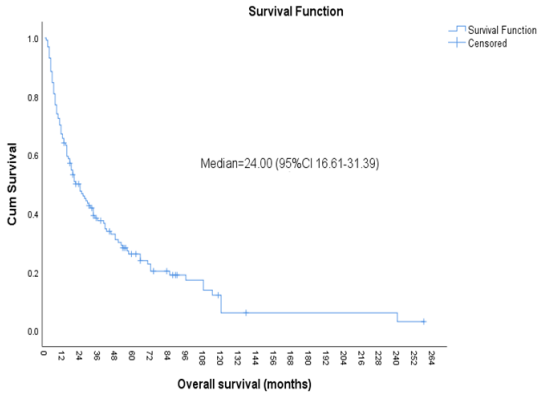

Figure (1): OS of 131 patients with RCC

Table.1: Patients characteristics of 131 patients with RCC

Characteristic	Number (131)	%
Age (years) (median 56)		
< 40	15	11.5
40-60	63	48.1
> 60	53	40.5
Sex		
Male	80	61.1
Female	51	38.9
Smoking		
No	103	78.6
Yes	28	21.4
Comorbidities		
Negative	**54**	**41.2**
positive	**77**	**58.8**
HTN	44	33.6
DM	25	19.1
HCV infection	28	21.4
Associated renal disease	11	8.4
Others *	15	11.5
Family history		
Negative	118	90.1
Positive	13	9.9
ECOG PS		
≤1	91	69.5
>1	40	30.5
BMI		
< 25	18	13.7
25-29.9	37	28.2
≥30	44	33.6
Unknown	32	24.4
Presentation		
Asymptomatic	**16**	**12.2**
Symptomatic	**115**	**87.8**
Loin pain	67	51.1
Hematuria	41	31.3
Symptomatic metastases	24	18.3
Constitutional symptoms	9	6.9
Hg		
≥ LLLRR	72	55.0
< LLLRR	59	45.0
Neutrophil		
≤ULLRR	123	93.9
> ULLRR	8	6.1
Platelet		
≤ ULLRR	125	95.4
> ULLRR	6	4.6
Albumin		
Normal	124	94.7
Hypoalbuminemia	7	5.3
Creatinine		
Normal	110	84.0
Abnormal	21	16.0
Calcium		
≤ ULLRR	16	12.2
Unknown	115	87.8
LDH		
≤ 1.5 of ULLRR	5	3.8
> 1.5 of ULLRR	2	1.5
Unknown	124	94.7

* Other comorbidities were cardiac diseases, goiter, gout, SLE (systemic lupus erythematosus), vitiligo and tuberous sclerosis.

-Association between multiple comorbidities were common in our study and some patients presented with multiple symptoms.

-(HTN) hypertension, (DM) Diabetes mellitus, (HCV) hepatitis C virus , (ECOG PS) Eastern Cooperative Oncology Group performance status, (BMI) Body mass index, (Hg) hemoglobin, (ULLRR) upper limit of laboratory reference range, (LLLRR) Lower limit of laboratory reference range, (LDH) lactate dehydrogenase.

Table.2: Tumor characteristics of 131 patients with RCC

Characteristic	Number (131)	%
Side		
Right	58	44.3
Left	72	55.0
Bilateral	1	0.8
N of renal lesions		
Single	126	96.2
Multiple	5	3.8
Size		
≤10 cm	78	59.5
> 10 cm	53	40.5
T stage		
T1	34	26.0
T2	55	42.0
T3	30	22.9
T4	12	9.2
N stage		
N0	85	64.9
N1	46	35.1
M stage		
M0	70	53.4
M1	61	46.6
TNM staging		
Stage I	17	13.0
Stage II	21	16.0
Stage III	31	23.7
Stage IV	62	47.3
Pathological types		
CcRCC	**75**	**57.3**
Non -ccRCC	**54**	**41.2**
PRCC	22	16.8
X.p 11.2 translocation RCC	11	8.4
ChRCC	7	5.3
Mucinous tubular and spindle cell carcinoma	4	3.1
CDC	2	1.5
RMC	1	0.8
Unclassified	7	5.3
Mixed ccRCC and non-ccRCC	**2**	**1.5**
Mixed clear and papillary	1	0.8
Mixed clear and x.p 11.2 translocation	1	0.8
Grade		
1	8	6.1
2	37	28.2
3	31	23.7
4	16	12.2
Unknown	39	29.8
LVE		
Absent	127	96.9
Present	4	3.1
Rhabdoid or sarcomatoid features		
Absent	113	86.3
Present	18	13.7

-(CcRCC) clear cell renal cell carcinoma, (PRCC) papillary renal cell carcinoma, (ChRCC) chromophobe renal cell carcinoma, (CDC) collecting duct carcinoma, (RMC) renal medullary carcinoma, (LVE) lymphovascular emboli.

Table.3: Prognostic factors affecting OS of 131 patients with RCC

Factor	Median OS (months)	Univariate analysis		Multivariate analysis	
		HR CI 95%	P value	HR CI 95%	P value
Age					
<40	36	1.415	**0.027***	1.767	**0.001***
40-60	25	(1.041-1.924)		(1.254-2.489)	
>60	19				
Sex		0.924			
Male	17	(0.622-1.372)	0.694		
Female	28				
Smoking		0.922			
No	24	(0.577-1.474)	0.734		
Yes	17				
Comorbidities		0.894			
Negative	18	(0.607-1.317)	0.570		
Positive	24				
HTN					
Absent	20	1.012	0.953		
Present	24	(0.674-1.520)			
DM					
Absent	24	1.002	0.994		
Present	19	(0.608-1.651)			
HCV infection					
Absent	24	0.719	0.180		
Present	20	(0.443-1.165)			
Associated renal disease					
Absent	24	0.712	0.392		
Present	9	(0.327-1.551)			
Family history					
Negative	20	0.605	0.154		
Positive	48	(0.303-1.208)			
ECOG PS					
≤1	34	3.285	**<0.001****	2.841	**0.001***
>1	7	(2.142-5.038)		(1.499-5.385)	
BMI					
<25	9	0.931			
25-29.9	18	(0.751-1.154)	0.513		
≥30	34				
Unknown	15				
Presentation					
Asymptomatic	19	1.100	0.767		
Symptomatic	24	(0.587-2.059)			
Loin pain			0.100		
Absent	30	1.387			
Present	18	(0.939-2.049)			
Hematuria					
Absent	17	.636	**0.032***	1.255	0.319
Present	42	(0.420-0.962)		(0.803-1.963)	
Constitutional symptoms					
Absent	24	1.982	0.065		
Present	6	(0.958-4.103)			
Hg					
≥LLLR	41	2.154	**<0.001****	1.851	**0.004***
<LLLRR	12	(1.458-3.181)		(1.851-1.213)	
Neutrophil					
≤ULLRR	24	2.693	**0.013***	0.789	0.600
>ULLRR	3	(1.237-5.863)		(0.325-1.915)	
Platelet					
≤ULLRR	24	2.190	0.090		
>ULLRR	3	(0.885-5.421)			
Albumin					
Normal	24	1.816	0.129		
Hypoalbuminemia	4	(0.840-3.929)			

Creatinine					
Normal	24	1.472	0.149		
Abnormal	15	(0.871-2.488)			
LDH					
≤1.5 of ULLRR	7	.612	**0.025***	0.783	0.303
>1.5 of ULLRR	3	(0.398-0.941)		(0.491-1.247)	
Unknown	24				
Side					
Right	30	1.434	0.068		
Left	18	(0.974-2.112)			
Bilateral	6				
Size					
≤10 cm	24	1.263	0.238		
>10 cm	21	(0.857-1.861)			
T stage					
T1	33	1.485	**0.001***	1.108	0.490
T2	29	(1.180-1.869)		(0.827-1.485)	
T3	19				
T4	4				
N stage					
N0	34	2.247	**<0.001****	1.098	0.694
N1	11	(1.491-3.386)		(0.691-1.745)	
M stage					0.254
M0	48	3.309	**<0.001****	1.677	
M1	11	(2.164-5.061)		(0.690-4.075)	
TNM stage					
Stage 1	108				
Stage II	53	1.928	**<0.001****	.971	0.896
Stage III	19	(1.543-2.410)		(0.623-1.512)	
Stage IV	11				
Pathology					
CcRCC	33	1.615	**0.010***	2.460	**<0.001****
Non- ccRCC	15	(1.123-2.322)		(1.572-3.850)	
Mixed	4				
Grade					
I	72				
2	48	1.574		1.582	
3	28	(1.349-1.837)	**<0.001****	(1.315-1.903)	**<0.001****
4	8				
Unknown	10				
LVE					
Absent	33	0.933	0.906		
Present	21	(0.295-2.951)			
Rhabdoid or sarcomatoid features					
Absent	28	2.475	**0.001***	1.964	**0.020***
Present	8	(1.475-4.154)		(1.113-3.467)	

* P value ≤ 0.05 (significant), **P value < 0.001 (highly significant).

-Calcium level was not studied as a prognostic factor as no cases with hypercalcemia were reported in current study.

-(HTN) hypertension, (DM) Diabetes mellitus, (HCV) hepatitis C virus, (ECOG PS) Eastern Cooperative Oncology Group performance status, (BMI) Body mass index, (Hg) hemoglobin, (ULLRR) upper limit of laboratory reference range, (LLLRR) Lower limit of laboratory reference range, (LDH) lactate dehydrogenase, (ccRCC) clear cell renal cell carcinoma, (LVE) lymphovascular emboli.

Discussion:

The commonest malignant tumor of the kidney is RCC [12]. Risk categorization for the patients is an important issue as it allows prediction of tumor behavior and patient prognosis; and therefore, selection of the most suitable therapeutic option and follow up schedule for each category [13].

It was evident in current retrospective study which analyzed 131 patients that the prognosis of RCC was extremely variable. The median OS was 24 months (CI 16.61-31.39) thus we evaluated prognostic factors for RCC patients.

Starting with demographic factors, the median age of our patients was 56 years. Age was not an established prognostic factor and was not incorporated in many studies for RCC prognostic factors. In current study, increasing age had a statistically significant negative correlation with OS in univariate analysis (P: 0.027), and it was independent prognostic factor in multivariate analysis. Kucuk et al. demonstrated similar results [14].

Male to female ratio was 1.6:1. We observed that male patients had lower median OS than females; however, gender was not significant prognostic factor in univariate analysis. Palacios et al. observed that male patients had lower OS with a statistically significant prognostic value [15].

Smoking was reported in 21.4% of cases that differed from results reported by Artyukhov et al. as smoking was presented in 49% of cases in their study [16]. The difference between both studies may be related to different social habits between countries. Smoking was associated with lower median OS in present study with no statistically significant correlation in univariate analysis. Kabaria, Klaassen, and Terris reported that cancer specific mortality was increased among tobacco exposure in RCC patients [17].

Associated Comorbidities were presented in 58.8 % in the current study. Hypertension, HCV infection, DM, and associated renal diseases were the commonest and this was different from Pal et al. who reported that hypertension, cardiovascular diseases and DM were the commonest comorbidities in their study [18]. In present study patients with DM had lower median OS than their counterparts with no significant prognostic value in univariate analysis. Several studies reported that RCC patients with DM had poorer survival compared with those non-diabetic counterparts with a significant prognostic value [19]. HCV infection was also associated with lower median OS with no significant prognostic value in univariate analysis. Interference with the activation of innate and adaptive immune responses with HCV infection may be the causing factor [20].

Most of patients were symptomatic at presentation in 87.8% of the cases which was similar to what was observed by Zhang et al. [21], but it differed from results reported by Grivas et al. where at diagnosis 50% of cases were asymptomatic [13]. In general, there was no significant correlation between the presence of symptoms and OS in univariate analysis. Surprisingly, on analyzing the correlation between hematuria and OS, we reported that the presence of hematuria was associated with improvement of OS with a statistically significant correlation (P: 0.032) but no significance in multivariate analysis. On the other hand, the presence of constitutional symptoms or loin pain was associated with lower median OS with no significant prognostic value in univariate analysis. That may be explained as hematuria is an alarming symptom causing early diagnosis. While, Yap et al. reported different outcomes as that presence of symptoms in general and systemic constitutional symptoms specifically were associated with worse prognosis with a significant prognostic value. Regarding local symptoms, they reported that palpable abdominal mass was the significant independent prognostic factor for lower OS [22].

Patients ECOG PS is the most important clinical prognostic factor for RCC and it was mentioned in University of California Los Angeles Integrated Staging System (UISS), the Memorial Sloan Kettering Cancer Center (MSKCC), and International Metastatic RCC Database Consortium (IMDC) scoring systems [23]. In present study, most of patients presented with good ECOG PS ≤1 (69.5%). Poor ECOG PS (>1) was associated with lower OS with a highly significant prognostic value in univariate analysis (P< 0.001), and it was independent prognostic factor in multivariate analysis. Basal et al. reported also the bad prognosis of poor ECOG PS with a statistically significant value [24].

Obese patients (BMI≥ 30) represented 33.6% in our study. It was evident that median OS was higher in obese patients and the lowest survival was observed in patients with normal weight, but not statistically significance in univariate analysis. Our results were in accordance with that reported by Martini et al. who documented that obese patients had higher OS than the non-obese counterparts. BMI was proved to have a prognostic significance and was included in the Emory risk scoring model [25].

A lot of laboratory findings emerged to have a prognostic significance in RCC, the most important are hematological indices and inflammatory markers thus were incorporated in MSCKK and IMDC scoring system [26]. We reported that Hg, neutrophil, platelet, albumin, and creatinine levels were abnormal in 45%, 6.1%, 4.6 %, 5.3%, and 16% respectively. Lactated dehydrogenase and calcium levels were not recorded in most cases. That was approximately comparable to Latif and Selim who reported that Hg and platelet levels were abnormal in 35.1% and 10.8% respectively. However, neutrophil and albumin levels were abnormal in 40.5% and 21.6% of their patients respectively [9]. That difference may be attributed to selective criteria for the patients as all patients were metastatic in their study.

In univariate analysis of the previous laboratory factors, anemia was associated with lower OS with a highly statistical significance (P< 0.001), it was independent prognostic factor in multivariate analysis. Neutrophilia and LDH level >1.5 ULLRR were associated with lower OS with a statistically significant correlation (P: 0.013 and 0.025 respectively) in

univariate analysis with no statistically significance in multivariate analysis. Thrombocytosis and hypoalbuminemia were associated with lower median OS with no significant prognostic value in univariate analysis. Our results were close to results reported by Latif & Selim who studied the prognostic significance for hematological indices, inflammatory markers, and albumin level [9]. Patients with elevated serum creatinine had lower median OS with no prognostic significance in univariate analysis. Palacios et al. reported that there was a statistically significant negative correlation between glomerular filtration rate and risk for cancer specific mortality but the risk disappears after adjustment of relevant tumor characteristics [15].

Regarding anatomical factors; most of patients (96.2%) presented with a single renal lesion. Fifty-nine percent of patients had tumors ≤10 cm. Early T stages (T1,2) were the commonest in our study that were presented in 26 % and 42% respectively. Regional LN metastasis and distant metastasis were presented in 35.1% and 46.6% of cases respectively. Stage IV was the commonest stage in our study that was presented in 47.3%. Kucuk et al. reported different descriptive criteria as stage I was the commonest in their study (53.9%) followed by stage III (24.5%), regional LN and distant metastasis were not frequent in their study that were presented in 5.9% and 9.8% respectively [14]. It is worth to be mentioned that most of patients attended to our department were metastatic either from the start or after failure which led to apparently increased incidence of metastasis and higher stages in our study.

Studies proved that TNM staging system had the most predictive prognostic value for RCC thus incorporated in UISS and size, stage, grade and necrosis (SSIGN) models followed by the tumor size that also proved a significant value and was added to SSIGN model [23]. In present study patients with large sized tumors (>10 cm) had a lower median OS with no statistically significant correlation in univariate analysis. T stage had a statistically significant negative correlation with OS (P: 0.001) while the presence of regional LN or distant metastasis and advanced TNM stages had a highly statistically significant negative correlation with OS (P <0.001) in univariate analysis. However, the previous anatomical factors were not independent prognostic fcators in multivariate analysis. Kucuk et al. proved the prognostic significance for previous described anatomical factors [14].

Analyses of histological factors revealed that ccRCC was the most common reported pathology followed by pRCC. Recorded tumor grades showed that GII was the most frequent recorded grade followed by GIII in 28.2% and 23.7% of cases respectively. Lymphovascular invasion, rhabdoid and /or sarcomatoid features were uncommon that were presented in 3.1 % and 13.7 % respectively. In agreement with Kuthi et al., but they reported that GII were the most frequent reported grade followed by G IV [27].

Pathological type of RCC was a significant prognostic factor for OS in univariate analysis (P: 0.010) and it was independent prognostic factor in multivariate analysis. Lower median OS was observed with mixed tumors followed by non-ccRCC and the highest survival was found with ccRCC. That differed from results reported by Palacios et al. who observed that ccRCC increased hazard of cancer specific mortality in their study [15]. In current analysis tumor grades had a highly statistically significant negative correlation with OS in univariate analysis (P<0.001) and it was independent prognostic factor in multivariate analysis. Presence of rhabdoid and /or sarcomatoid features was a significant prognostic factor for OS in univariate analysis (P: 0.001) with a prognostic significance in multivariate analysis. Kuthi et al. studied the correlation between tumor grade, rhabdoid and /or sarcomatoid features and cancer specific survival and a statistically significant correlation was found [27]. In present study, patients with positive LVE had a lower median OS with no statistically prognostic significance in univariate analysis. Chang et al. proved that the presence of LVE associated with worse prognosis with a statistically significance [28]. In general tumor grade is considered the strongest histological prognostic factor and thus was applied in UISS and SSIGN scoring systems [23].

Conclusion:

The identification of prognostic factors in patients with RCC had been considered an area of increasing interest. Our study proved the value of demographic, clinical, anatomical, and histological prognostic factors for RCC. Two years, 5 years, and 10 years OS were 50%, 26%, and 11% respectively in our patients. Moreover, there were limitations in our retrospective study. First, some prognostic factors like calcium and LDH levels were not recorded in most of patients. Second, the small sample size in some arms of prognostic factors as one arm may be not frequent. Lastly, the study sample size was a limitation in our case series as it was a single center database. Further future prospective studies with large sample size are encouraged.

Compliance with ethical standards:

Ethical approval was obtained from Institutional Research Board (IRB) at the Faculty of Medicine, Mansoura University, Egypt (MS.19.11.909). All procedures were done in accordance with the current revision of Helsinki Declaration of medical research involving human subjects.

Conflict of interest:

The authors declare that no conflict of interest to disclose.

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References:

1. Medina-Rico M, Ramos HL, Lobo M et al. Epidemiology of renal cancer in developing countries: Review of the literature. Canadian Urological Association Journal 2018; 12: E154.
2. Palumbo C, Pecoraro A, Knipper S et al. Contemporary age-adjusted incidence and mortality rates of renal cell carcinoma: analysis according to gender, race, stage, grade, and histology. European Urology Focus 2020.
3. Ghosn M, Jaloudi M, Larbaoui B et al. Insights into the epidemiology of renal cell carcinoma in North Africa and the Middle East. Pan Arab Journal of Oncology 2015; 8.
4. Capitanio U, Bensalah K, Bex A et al. Epidemiology of renal cell carcinoma. European urology 2019; 75: 74-84.
5. Hsieh JJ, Purdue MP, Signoretti S et al. Renal cell carcinoma. Nature reviews Disease primers 2017; 3: 1-19.
6. Klatte T, Rossi SH, Stewart GD. Prognostic factors and prognostic models for renal cell carcinoma: a literature review. World journal of urology 2018; 36: 1943-1952.
7. Erdogan S, Ozcan A, Truong LD. Molecular Pathology of Kidney Tumors. In Kidney Cancer. Springer 2020; 375-398.
8. Larroquette M, Peyraud F, Domblides C et al. Adjuvant therapy in renal cell carcinoma: Current knowledges and future perspectives. Cancer Treatment Reviews 2021; 97: 102207.
9. Latif RMA, Selim KF. Effect of Initial Cytoreductive Nephrectomy with Target Therapy versus Target Therapy Alone in Metastatic Renal Cell Carcinoma: A Single Institutional Study. Indonesian Journal of Cancer 2019; 13: 35-43.
10. Mori K, Mostafaei H, Miura N et al. Systemic therapy for metastatic renal cell carcinoma in the first-line setting: a systematic review and network meta-analysis. Cancer Immunology, Immunotherapy 2021; 70: 265-273.
11. Siegel RL MK, Jemal A. Cancer statistics. CA Cancer J Clin 2016; 66: 7–30
12. Lorente D, Trilla E, Meseguer A et al. Systematic review of renal carcinoma prognostic factors. Actas Urológicas Españolas (English Edition) 2017; 41: 215-225.
13. Grivas N, Kafarakis V, Tsimaris I et al. Clinico-pathological prognostic factors of renal cell carcinoma: A 15-year review from a single center in Greece. Urology annals 2014; 6: 116.
14. Kucuk U, Palo E, Sezer O et al. Significance of TNM staging, demographic and histologic features in predicting the prognosis of renal cell carcinoma. Acta chirurgica Belgica 2015; 115: 202-207.
15. Palacios DA, Zabor EC, Munoz-Lopez C et al. Does reduced renal function predispose to cancer-specific mortality from renal cell carcinoma? European Urology 2021; 79: 774-780.
16. Artyukhov I, Zukov R, Reshetnikov V et al. Lifestyle risk factors in the development of kidney cancer: A Russian experience. Serbian Journal of Experimental and Clinical Research 2018; 19: 35-40.
17. Kabaria R, Klaassen Z, Terris MK. Renal cell carcinoma: links and risks. International journal of nephrology and renovascular disease 2016; 9: 45.
18. Pal SK, Ghate SR, Li N et al. Real-world survival outcomes and prognostic factors among patients receiving first targeted therapy for advanced renal cell carcinoma: a seer–Medicare database analysis. Clinical genitourinary cancer 2017; 15: e573-e582.
19. Li Y, Hu L, Xia Q et al. The impact of metformin use on survival in kidney cancer patients with diabetes: a meta-analysis. International urology and nephrology 2017; 49: 975-981.
20. Tsimafeyeu I, Gafanov R, Protsenko S et al. Nivolumab in patients with metastatic renal cell carcinoma and chronic hepatitis C virus infection. Cancer Immunology, Immunotherapy 2020; 69: 983-988.
21. Zhang BY, Thompson RH, Lohse CM et al. A novel prognostic model for patients with sarcomatoid renal cell carcinoma. BJU international 2015; 115: 405-411.
22. Yap NY, Ng KL, Ong TA et al. Clinical prognostic factors and survival outcome in renal cell carcinoma patients-A Malaysian single centre perspective. Asian Pacific Journal of Cancer Prevention 2013; 14: 7497-7500.
23. B. Escudier CP, M. Schmidinger, N.Rioux-Leclerq, A. Bex, V. Khoo, V. Gruenwald, S. Gillessen and A. Horwich. Renal Cell Carcinoma: ESMO Clinical Practice Guidelines. Ann Oncol 2019; 30: 706-720.
24. Basal FB, Karacin C, Bilgetekin I, Oksuzoglu OB. Can Systemic Immune-Inflammation Index Create a New Perspective for the IMDC Scoring System in Patients with Metastatic Renal Cell Carcinoma? Urologia Internationalis 2021; 105: 666-673.
25. Martini DJ, Liu Y, Shabto JM et al. Novel risk scoring system for patients with metastatic renal cell carcinoma treated with immune checkpoint inhibitors. The oncologist 2020; 25: e484-e491.
26. Guida A, Le Teuff G, Alves C et al. Identification of International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) intermediate-risk subgroups in patients with metastatic clear-cell renal cell carcinoma. Oncotarget 2020; 11: 4582.
27. Kuthi L, Jenei A, Hajdu A et al. Prognostic factors for renal cell carcinoma subtypes diagnosed according to the 2016 WHO renal tumor classification: a study involving 928 patients. Pathology & Oncology Research 2017; 23: 689-698.
28. Chang Y, An H, Xu L et al. Systemic inflammation score predicts postoperative prognosis of patients with clear-cell renal cell carcinoma. British journal of cancer 2015; 113: 626-633.