

The outcomes of renal cell carcinoma in a single tertiary care facility in Saudi Arabia

Lujain Alqurashi, Marwan Al-Hajeili, Ehab Alsayyed¹, Budoor Salman, Hibatallah Mashat, Rana Bokhary²

Departments of Medicine, ¹Urology and ²Pathology, King Abdulaziz University, Jeddah, Saudi Arabia

Abstract

Background: Amidst an era of rising malignancies worldwide, renal cell carcinoma (RCC) is the 7th most commonly detected, owing to 144,000 cancer-related deaths annually. Demographic knowledge of such cases in Saudi Arabia is poorly portrayed. According to the 2014 Saudi Cancer Registry, RCC has rated the 10th most common malignancy among males, posing a significant disease burden. Global studies have depicted a great discrepancy of 15 folds in the incidence of RCC among different countries, which is commonly attributed to variations in each countries development. We aimed to assess the overall survival (OS) and disease-free survival (DFS) in patients who underwent nephrectomy in our health-care facility.

Materials and Methods: This is a retrospective study done at a tertiary care facility of all cases of RCC as per the pathology department database for the period of 2007–2017. The OS and DFS were statistically determined using Stata/SE 15.0.

Results: Overall, 109 RCC patients were included in the study. Mean age at diagnosis was 53.8 (range: 24–89) years. Demographic data revealed a total of 71 (65.14%) males included in the study and 38 (34.86%) females. The OS at 2 years and 5 years was noted to be 95.3% and 92.6%, respectively. The DFS was found to be 90.8% at 2 years and 85.4% at 5 years. On multivariate analysis of the results, step-wise model was utilized to eliminate irrelevant variables affecting the OS, with a probability to eliminate variables with $P > 0.2$. Metastasis (M) was found to be a relevant variable (hazards ratio [HR]: 52.25 [$P = 0.003$]; 95% confidence interval [CI]: 3.75–728.88). On multivariate analysis of the DFS, variables were found to be significant which include gender (HR: 0.15 [$P = 0.063$]; 95% CI: 0.02–1.105), nationality (HR: 16.1 [$P = 0.034$]; 95% CI: 1.24–209.13), age at diagnosis (HR: 0.93 [$P = 0.031$]; 95% CI: 0.87–0.99), and pathological stage (T) (HR: 7.89 [$P = 0.003$]; 95% CI: 1.98–31.36).

Conclusions: Our results revealed a notable discrepancy in the 5-year OS and the 5-year DFS as compared to studies in the literature. However, our study was limited to a single center and the majority of our patients were diagnosed at a rather early stage. With the rising number of RCC cases worldwide and in Saudi, this further necessitates extensive disease surveillance for trends in all parameters.

Keywords: Kidney cancer, nephrectomy, renal cell carcinoma, staging

Address for correspondence: Dr. Lujain Alqurashi, King Abdulaziz University, P.O. Box 80200, Jeddah 21589, Saudi Arabia.

E-mail: lujainmalqurashi@gmail.com

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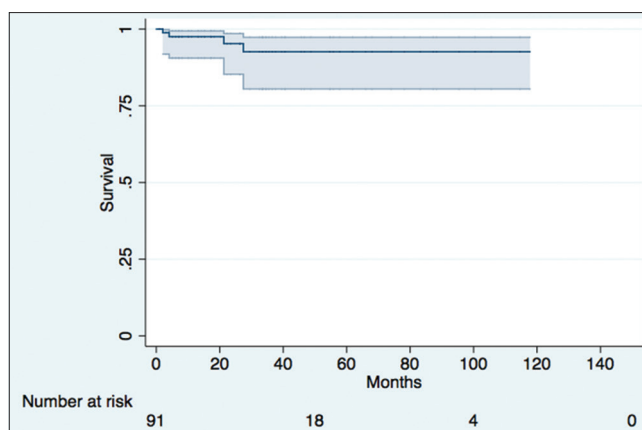
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INTRODUCTION

Amidst an era of rising detection of malignancies worldwide, renal cell carcinoma (RCC) is the 7th most commonly detected, owing to approximately 144,000 cancer-related deaths annually.^[1] According to the World Health Organization (WHO) classification of tumors, RCC constitutes the vast majority of all renal malignancies and are of putative renal tubular epithelium origin with histological subtypes that vary according to cytoplasmic and architectural features and tumor location. The most common histological subtypes are clear cell, papillary, and chromophobe. New entities of renal epithelial origin have emerged and have been described by the updated 2016 WHO classification. These include hereditary leiomyomatosis and RCC syndrome-associated RCC, succinate dehydrogenase-deficient RCC, tubulocystic RCC, acquired cystic RCC, and clear cell papillary RCC.^[2] RCC is variably impacted by several risk factors including smoking, obesity, hypertension, and specific syndromes of which Von Hippel–Lindau is the prevailing. Familial cases comprise 2%–3% of RCC and are associated with a two-fold higher risk among first-degree relatives.^[3,4]

A rise of 2%–3% in the 10-year incidence and mortality rates has been noted internationally with a 15-fold variation noted worldwide. The highest incidence rates are found in the Czech Republic followed by increasing levels in Northern and Eastern Europe, North America, and Australia as opposed to lower rates in Africa and Southeast Asia. Demonstration of stabilization of mortality trends has also been noted in most developed nations.^[5] Europe has the highest incidence in the world affecting 7.2–33.6/100,000 males and 3.4–15/100,000 females with an age-standardized incidence of 8.9–12.9/100,000 and 4.1–5.9/100,000 in males and females, respectively, as compared to the Middle East and Africa, the age-standardized incidence is 1.8–4.8/100,000 and 1.2–2.2/100,000 for males and females, respectively.^[6] According to Globocan's estimated cancer incidence, mortality, and prevalence report in 2012, the estimated incidence according to age-standardized rate (ASR) was found to be 6.0/100,000 and 3.1/100,000 in males and females, respectively. The estimated cancer deaths according to ASR were 2.5/100,000 in males and 1.2/100,000 in females.^[7]

According to the 2014 Saudi Cancer Registry, RCC has rated the 10th most common malignancy among males and 13th among female population, in which 193 (61.7%) males and 120 (38.3%) females were affected with a male-to-female ratio of 160:100. The median age at diagnosis was 56 years



Graph 1: Kaplan–Meier survival estimate

among males and 49 years among females. The ASR of incidence in males and females was found to be 2.7/100,000 and 1.4/100,000, respectively.^[8]

In a study that aimed to address the fundamental rise in kidney cancer incidence in a portion of the Saudi population over two decades, there was a notable increase in number of diagnosed cases of RCC. A paradigm shift of diagnosed cases to being incidental and of early stages has been noted globally and attributed to lowering the threshold of utilizing diagnostic imaging techniques resulting in advances in therapy.^[9]

The aim of this study is to identify epidemiologic data of RCC and to assess the overall survival (OS) and disease-free survival (DFS) in nonmetastatic patients who underwent radical and partial nephrectomy at a tertiary care facility in Jeddah, Saudi Arabia over a 10-year period.

MATERIALS AND METHODS

Study design

This is a retrospective study done at a tertiary care facility of all cases of RCC as per the pathology department database and electronic health-care systems for the period of 2007–2017. An institutional ethical clearance was obtained by the Unit of Biomedical Ethics at King Abdulaziz University. Confidentiality of the participant's data was maintained by encrypting the files and securing the devices which contained them.

Data collection

A total of 109 cases of RCC were collected, and the variables obtained were demographic data including date of birth, gender, and nationality. Histopathological features recruited comprised specimen type, histological subtype, tumor, node, metastasis staging, histopathological grading, type of grading system utilized, surgical margins, and

laterality. Other factors obtained were date of pathological diagnosis, type of surgical treatment offered, date of disease progression, metastasis based on radiological evidence, systemic treatment given, date of last follow-up, and vital status. Stata/IC 15.1 for Mac, (4905 Lakeway Dr, College Station, TX 77845, USA) was utilized for the statistical analysis.

RESULTS

Overall, 109 RCC patients were included in the study for analysis. The mean age at diagnosis was 53.88 ± 1.29 standard deviation ranging from 24 to 89 years. Demographic data revealed a total of 71 (65.14%) males included in the study and 38 (34.86%) females with 52 (47.71%) Saudi nationals and 57 (52.29%) non-Saudi cases. Histopathological features were analyzed and were summarized in Tables 1, 2 and Graph 1. The majority of pathological T stage in this study was pT1 (46.79%), with the majority being initially nonmetastatic (77.06%). The most prevalent subtype of RCC noted was clear cell (67.89%). Of the 109 patients recruited in this study, the OS at 2 years and 5 years was noted to be 95.3% and 92.6%, respectively. The DFS was found to be 90.8% at 2 years and 85.4% at 5 years. The median follow-up time was noted to be 13.16 months (95% confidence interval [CI]: 7.11–18.75). The Kaplan–Meier survival estimate is presented in the graph below.

Univariate analysis of the results showed gender to have a 6.5 times increase in the risk of death in females as compared to males. The pathological T stage univariate analysis showed a 5.8 folds increase in risk of death on progression from one T stage to another with a $P = 0.02$ (95% CI: 1.32–26.0). When analyzing the nodal status (N), a 4.03 increment has been noted with no significant P value. Metastatically positive cases based on radiological evidence [Table 3] revealed a 18-fold rise in hazards ratio (HR) with a $P = 0.01$ [Table 4] (95% CI: 1.85–174.66). Initial presentation with metastasis has also increased HR by 7.57 with a $P = 0.04$ (95% CI: 1.03–55.08). Of the 109 cases employed in our study, they all received surgical treatment in the form of total nephrectomy (74.31%) or partial nephrectomy (25.69%). Only one case was observed to receive systemic therapy in conjugate with surgical treatment. On univariate analysis of the DFS stage, T was found to be a significant factor with a HR of 3.81 and a $P = 0.003$ (95% CI: 1.59–9.102).

On multivariate analysis of the results, step-wise model was utilized to eliminate irrelevant variables affecting the

Table 1: Demographic data

	Frequency (%)
Total	109 (100)
Age at diagnosis±SD	53.88±1.2
Gender	
Male	71 (65.14)
Female	38 (34.86)
Nationality	
Saudi	52 (47.71)
Non-Saudi	57 (52.29)

SD: Standard deviation

Table 2: Histopathological characteristics

Characteristic	n (%)
Stage (T)	
T0	4 (3.67)
T1	51 (46.79)
T2	18 (16.51)
T3	35 (32.11)
T4	1 (0.92)
Lymph nodes (N)	
Nx	71 (65.14)
N0	29 (26.61)
N1	9 (8.26)
Metastasis (M)	
Mx	9 (8.26)
M0	84 (77.06)
M1	16 (14.68)
Grade	
Unknown 0	15 (13.76)
1	19 (17.43)
2	46 (42.20)
3	16 (14.68)
4	13 (11.93)
Type of cancer	
Clear cell	74 (67.89)
Papillary	15 (13.76)
Chromophobe	13 (11.93)
Cystic-solid	2 (1.83)
Medullary	1 (0.92)
Unclassified	4 (3.67)
Margins	
Positive	6 (5.50)
Negative	103 (94.50)

Table 3: Univariate and multivariate analyses of the overall survival

Variables	Univariate		Multivariate	
	HR	P	HR	P
Gender	6.5	0.10	-	-
Pathological T stage	5.8	0.02	-	-
Metastasis	18	0.01	52.25	0.003
Grade	0.94	0.88	0.437	0.1

HR: Hazards ratio

Table 4: Univariate and multivariate analyses of the disease free survival

Variables	Univariate		Multivariate	
	HR	P	HR	P
Gender	1.31	0.71	0.15	0.06
Nationality	6.08	0.09	16.1	0.03
Age at diagnosis	0.96	0.10	0.93	0.03
Pathological T stage	3.81	0.003	7.89	0.003

HR: Hazards ratio

OS, with a probability to eliminate variables with $P > 0.2$. On elimination technique, the variables found to be irrelevant included gender, nationality, age at diagnosis, stage (T), lymph nodes (N), grade, margins, and those initially presenting with metastasis. Metastasis (M) was found to be relevant with a HR of 52.25 and $P = 0.003$ (95% CI: 3.75–728.88). On application of the same step-wise elimination technique on multivariate analysis of the DFS, the variables found to be irrelevant included lymph nodes (N), metastasis (M), grade, margins, and those initially presenting with metastasis. Variables found to be significant include gender (HR: 0.15 [$P = 0.063$]; 95% CI: 0.02–1.105), nationality (HR: 16.1 [$P = 0.034$]; 95% CI: 1.24–209.13), age at diagnosis (HR: 0.93 [$P = 0.031$]; 95% CI: 0.87–0.99), and pathological stage (T) (HR: 7.89 [$P = 0.003$]; 95% CI: 1.98–31.36).

DISCUSSION

Our results revealed an OS of 95.3% at 2 years and 92.6% at 5 years and a DFS of 90.8% at 2 years and 85.4% at 5 years. According to SEER's RCC statistics between 2008 and 2014, the 5-year survival was 74.5%; 16% of that population was diagnosed with metastatic RCC with a 5-year survival of 11.6%. This supports our data which demonstrated a significant 18-fold rise in the OS's HR with a $P = 0.01$ on univariate analysis and a 52-fold rise with a $P = 0.003$ on multivariate analysis.^[9]

The discrepancy between our 5-year OS (92.6%) and SEER data OS of 74.5% is due to the inclusion of renal pelvis malignancies in their data; in addition, the majority of our patients were diagnosed at an early stage, and hence, requiring only surgical intervention in the forms of partial and total nephrectomy.^[8] RCC is of distinct importance in Saudi Arabia due to its ranking among the commonly noted malignancies and the acknowledgment of its increasing incidence according to a study done by Alkhateeb *et al.* Our study revealed a mean age at diagnosis of 53.88 with is in concordance with national figures.^[9,10]

CONCLUSION

Our results revealed a notable discrepancy in the 5-year OS and the 5-year DFS as compared to studies in the literature. However, our study was limited to a single center, and the majority of our patients were diagnosed at a rather early stage. Due to the noted increment in RCC cases worldwide and in Saudi, this further necessitates extensive disease surveillance for trends in all parameters of OS and DFS.^[5]

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Conflicts of interest

There are no conflicts of interest.

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