

## ORIGINAL RESEARCH

# Prevalence of Different Subtypes of Renal Cell Carcinoma among Patients who have Undergone Nephrectomy; Statistics of a Referral Medical Center in Iran

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**Abstract:** Renal cell carcinoma (RCC) is the third most common genitourinary cancer in the world, and has the highest mortality rates among these types of cancers. In the present cross-sectional assessment, the prevalence of RCC subtypes in a sample of Iranian patients diagnosed with RCC which have undergone nephrectomy surgery between years 2014 to 2019 in a referral medical center has been investigated. We have studied 68 patients, including 47 male and 21 female individuals with an average age of 55. The patients have been studied for demographic and pathologic information such as age, sex, tumor size, tumor subtype, TNM staging, Fuhrman nuclear grading, and other pathological information. The statistical analysis was done via SPSS software version 21. Quantitative data were examined by T test and qualitative data were assessed by Chi square test. As we observed in the results, the most common RCC subtype among these patients was clear cell 53%, followed by papillary 22% and chromophobe 19%, emphasizing the higher rates of chromophobe RCC compared to the statistics worldwide.

**Keywords:** Renal Cell Carcinoma; Nephrectomy; Pathology; Chromophobe Renal Cell Carcinoma; Clear Cell Renal Cell Carcinoma; Prevalence; Histology

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## 1. Introduction

The most common cancer of the kidney is renal cell carcinoma. It consists of different histologic subtypes (1, 2). RCC has the highest mortality rates among all genitourinary cancers. It also ranks the third most common genitourinary cancer worldwide (3). If diagnosed in the early stages, this cancer can be easily controlled by performing nephrectomy surgery. Nevertheless, a low percentage of patients still remain at risk of tumor recurrence (4). In addition, in patients with metastasis (mRCC), it is usually considered as an incurable disease. All RCC subtypes are different in prognosis and recurrence

rates. According to a study performed on 290 patients by Zhou H et al, results have shown that patients with clear cell-papillary RCC have been diagnosed in early stages when the tumor size is rather smaller. In addition, this particular subtype of RCC has not led to metastasis or cancer-specific death in any of the patients (5).

In another investigation on 840 patients by Lau WK et al, a significant difference in cancer-specific survival (CSS) and metastasis-free survival (MFS) rates among different RCC subtypes was observed. According to this research CSS and MFS for clear cell RCC are 89.1% and 88.6% respectively, for papillary RCC they are 95% and 93.8%, and for Chromophobe RCC they are both 100%. This study proves that prognosis of this cancer strongly depend on the RCC subtype (6).

The most common subtype of this cancer is clear cell (ccRCC) and it is the mostly fatal subtype of renal cancer (7).

According to a study by Lucca I et al, men are more likely to

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be diagnosed with renal cell carcinoma than women. And they usually have tumors with larger sizes and higher grade and stage (8).

In an assessment, Nicodemus KK et al studied 41,836 women. The results have shown that obesity and central accumulation of adipose tissue can be a risk factor for renal cancer in postmenopausal women (9).

Due to the inadequacy of statistics available on this matter among Iranian population, we attempted to conduct this survey. The current study aims to assess the prevalence of different subtypes of RCC in patients undergone nephrectomy surgery in Shohadae-Tajrish hospital during 2014 to 2019.

## 2. Materials and Methods

This cross-sectional study is conducted on a sample of 68 individuals (47 men and 21 women) with average age of 55 undergone nephrectomy surgery in Shohadae-Tajrish hospital. Subjects with clinically proven RCC were comprised the case group of the current survey.

Demographic and pathologic characteristics were gathered from all the participants. Pathologic characteristics like tumor subtype, TNM staging, Fuhrman nuclear grade, tumor size, neurolymphovascular invasion, necrosis, reactive lymph nodes, and surgical margins were measured.

The statistical analysis was done via SPSS software version 21. Quantitative data were examined by T test. Moreover, Chi square test was applied for qualitative variables.

## 3. Results

In this cross-sectional survey, 68 patients with average age of 55 were studied. The majority of the participants (approximately 69%) were men. 59 patients (87%) had undergone radical nephrectomy and the other 9 (13%) had undergone partial nephrectomy. The frequency of Fuhrman grading between men included in this study were as follows: 4 men (13%) presented grade I, 14 men (45%) grade II, 9 men (29%) grade III, and 4 men (13%) presented grade IV. In 21 patients of this group, (68%) necrosis was present, and in 10 patients (32%) necrosis was not identified. Margins of the resected tissue were tumor-free in 31 cases (67%) and in 15 cases (33%) margins were involved by the tumor. In 18 cases (86%) no sarcomatoid or rhabdoid feature were seen, but in 3 cases (14%) at least one of these features were present. Also, in 17 cases (61%) no reactive lymph node were detected in the resected tissue, in 10 cases (35.7%) only one lymph node, and in 1 man (3.3%) 3 lymph nodes were detected.

Women included almost 31% of the participants. Among all the 21 women studied, majority of them were in the postmenopausal age group. The frequency of Fuhrman grading between women in this survey were as follows: 1 patient (5.6%) presented grade I, 11 patients (61%) grade II, 5 pa-

tients (27.8%) grade III, and 1 patient (5.6%) presented grade IV. In 6 cases of this group (40%) necrosis was present, and in 9 cases (60%) necrosis was not identified. Margins of the resected tissue were tumor-free in 15 cases (75%) and in 5 cases (25%) margins were involved by the tumor. In 9 cases (90%) no sarcomatoid or rhabdoid feature were seen, but in 1 woman (10%) rhabdoid features were present. Also in 7 cases (77.8%) no reactive lymph node were detected in the resected tissue, in 1 woman (11.1%) only one lymph node, and in 1 woman (11.1%) 2 lymph nodes were detected.

Information about 64 patients who have shown clear cell, papillary and chromophobe subtypes are presented in table 1. Among the other 4 patients, 2 of them were presented with translocation carcinoma. Both were female with the average age of 20. They both had grade II tumors, with mean size of 5.7 cm. In one of them, the margins were tumor-free and in the other patient, they were involved by tumor. In addition, in one of these patients no lymph node were identified, and in the other one only 1 node was detected.

The patient with collecting duct carcinoma was a 57 year-old man with mean tumor size of 4.5 cm. Necrosis was present in the tissue resected, and margins were involved by tumor. The last patient was a 38 year-old man with unclassified RCC, with mean tumor size of 16 cm. The tumor was in grade IV. Necrosis, sarcomatoid features and lymphovascular invasions were present. The margins were also involved.

In general, 36 patients (53%) have presented the clear cell subtype, followed by papillary in 15 patients (22%), chromophobe in 13 patients (19%), translocation carcinoma in 2 patients (3%), collecting duct carcinoma in 1 patient (1.5%), and unclassified RCC in 1 patient (1.5%). We can see the significant difference between the frequencies of RCC subtypes in our patients and the universal statistics, especially in chromophobe RCC.

## 4. Discussion

To conclude, this research showed that among these 68 patients the most common subtypes are clear cell (53%), followed by papillary (22%) and chromophobe (19%). Altogether 5 patients (10.25%) presented grade I tumor, 25 patients (51%) grade II, 14 patients (28.5%) grade III, and 5 patients (10.25%) presented grade IV tumor. In 27 patients (58.6%) necrosis was seen. In 46 patients (70%) margins of the resected tissue were tumor-free. Neurolymphovascular invasion was identified in 12 patients (21.4%). Sarcomatoid features were present in 3 patients (9.6%) and rhabdoid features were present in 2 patients (6.4%). Moreover, in 13 patients (35%) the tissue contained lymph nodes. We can clearly observe that the male population diagnosed with this cancer is almost three times as big as the female population regardless of the RCC subtype.

**Table 1:** Pathologic characteristics of study patients.

Characteristic	Clear Cell (n=36)	Papillary (n=15)	Chromophobe (n=13)
Mean age (year)	55	61.3	53.3
Sex (M/F)	M=25 (69.4%) F=11 (30.6%)	M=10 (66.7%) F=5 (33.3%)	M=10 (76.9%) F=3 (23.1%)
Operation	RN=31 (86.1%) PN=5 (13.9%)	RN=12 (80%) PN=3 (20%)	RN=12 (92.3%) PN=1 (7.7%)
Mean tumor Size (cm)	6.5	7.4	10.1
Furman Grade	G1=5 (14.7%) G2=17 (50%) G3=9 (26.5%) G4=3 (8.8%)	G1=0 G2=3 (42.8%) G3=3 (42.8%) G4=1 (14.4%)	G1=0 G2=3 (75%) G3=1 (25%) G4=0
Necrosis	Present=10 (43.5%) Not seen=13 (56.5%)	Present=7 (77.8%) Not seen=2 (22.2%)	Present=6 (60%) Not seen=4 (40%)
Margins	Tumor free=26 (72.2%) Involved=10 (27.8%)	Tumor free=10 (76.9%) Involved=3 (23.1%)	Tumor free=9 (69.2%) Involved=4 (30.8%)
NLV invasion	Present=4 (18.2%) Not seen=27 (81.8%)	Present=4 (30.8%) Not seen=9 (69.2%)	Present=2 (20%) Not seen=8 (80%)
Lymph nodes	Present=4 (20%) Not seen=16 (80%)	Present=2 (25%) Not seen=6 (75%)	Present=5 (83.3%) Not seen=1 (16.7%)

M: male; F: female; RN: radical nephrectomy; PN: partial nephrectomy; NLV: Neurolymphovascular invasion.

In an investigation on 3062 RCC patients by Leibovich BC throughout 33 years, the results have shown that clear cell RCC patients comprised 80.5% of all the patients. The percentage for papillary RCC and chromophobe RCC patients were 14.3 and 5.2 respectively (10). However, we have found that only 53% of our patients were diagnosed with clear cell RCC, 22% with papillary and 19% with chromophobe RCC. The ratio between the different subtypes of this cancer is the main difference seen in our results. According to a study conducted by Lipworth L et al on 1549 American patients with RCC, there was a significant difference in distribution of RCC subtypes among white and black people. In comparison with clear cell RCC, there was a higher chance patients with papillary RCC were black and of male sex. On the contrary, majority of the patients with chromophobe RCC were of female sex. Overall, clear cell RCC subtype comprised 72.9% among all the tumors. For papillary RCC and chromophobe RCC the percentages were 15.7% and 5% respectively (11, 12).

In a survey conducted by Wu J et al on 2149 Chinese patients with clear cell, papillary and chromophobe renal cell carcinoma results show that compared to clear cell RCC patients, there was a higher chance for chromophobe RCC patients to be female, younger and to have larger tumor size (13). According to this study, chromophobe RCC patients tend to be younger and have tumors with larger diameters than clear cell and papillary RCC patients; which matches the statistics throughout the world. Nevertheless, as we can see in table 1 women comprise only 23.1% of the chromophobe RCC patients; which is another difference we found, compared to the statistics worldwide.

Regarding the fact that RCC does not respond well to neither radiation therapy nor chemotherapy, there remains mainly two modes of treatment: immunotherapy and nephrectomy surgery which can be performed as radical or partial nephrectomy (14, 15).

Nephron-sparing nephrectomy, also known as partial nephrectomy, can prevent from renal insufficiency and hypertension even in the elderly. It also may cause lower other-cause mortality rates (16).

## 5. Conclusion

We recommend more extensive research be conducted on the Iranian population to verify the statistics found in the current study. In addition, on the assumption that the pattern of distribution of the RCC subtypes worldwide is different from Iran, further investigations must be performed.

## 6. Appendix

### 6.1. Acknowledgements

This research project has been approved by the ethics committee of Shahid Beheshti University of medical sciences. (Ethics code: IR.SBMU.MSP.REC.1396.779)

### 6.2. Author contribution

All the authors have the same contribution.

### 6.3. Funding/Support

None.



#### 6.4. Conflict of interest

All authors declare that there is no conflict of interest in this study.

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