

# Gender-related Differences in Surgically Treated Patients with Renal Cell Carcinoma

## Cerrahi Olarak Tedavi Edilen Böbrek Tümörü Hastalarının Cinsiyete Özgü Farklılıkları

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### What's known on the subject? and What does the study add?

The gender-related differences of the patients who have surgically treated renal cell carcinoma are already known for the Europe and America. However, in the literature, there is no information about these differences for Turkish population. Our study may guide future studies with similar concept with more patients in our population.

### Abstract

**Objective:** The aim of the study was to investigate gender-specific differences in the Turkish patients with renal cell carcinoma (RCC) undergoing radical or nephron-sparing nephrectomy and compare the results with those in other regions.

**Materials and Methods:** Data of 76 patients, who were clinically diagnosed with RCC and underwent radical or nephron-sparing nephrectomy from January 2011 to August 2017, were retrospectively evaluated. Age and gender of the patients and the size, histological type, grade and pathological stage of the tumors were recorded. A chi-square test was used for comparing categorical variables, whereas the Student's t-test was used for the same purpose in the continuous variables.

**Results:** Of the 67 patients, 39 (58.2%) were male and 28 (41.8%) were female; male-to-female ratio was 3:2. The mean age of the male and female patients was 63.4±11.7 years and 59.3±14.3 years, respectively and the mean tumor size was 5.7 and 5.3 cm, respectively. There were differences in mean age, tumor size and Fuhrman grade, however, none of them reached the level of statistical significance. Twenty four of the male and 25 of the female patients had low-stage, 15 of the male and 3 of the female patients had high-stage disease. Thus, the male patients had higher stage disease than the female patients and the difference was statistically significant (p=0.011).

**Conclusion:** Turkish women with RCC had significantly lower stage disease than Turkish men, although grade and size of the tumor did not present a statistically significant difference. The results were similar with other European studies.

**Keywords:** Renal cell carcinoma, Gender, Difference, Radical, Nephron sparing, Nephrectomy

### Öz

**Amaç:** Çalışmamızın amacı, radikal ya da nefron koruyucu cerrahi ile tedavi edilmiş renal hücreli karsinomlu (RHK) hastalarımızın cinsiyete özgü farklılıklarını değerlendirmek ve bunu diğer bölgeler ile karşılaştırmaktır.

**Gereç ve Yöntem:** Ocak 2011 ile Ağustos 2017 arasında klinik olarak RHK tanısı almış ve radikal veya nefron koruyucu nefrektomi operasyonu geçirmiş olan 76 hastanın verileri retrospektif olarak gözden geçirildi. Hastaların yaşları ve cinsiyetleri ile tümörlerinin boyutu, histolojik tipi, derecesi ve patolojik evreleri bulundu. Kategorik değişkenlerin değerlendirilmesinde ki-kare testi, sürekli değişkenlerin değerlendirilmesinde ise Student's t-testi kullanıldı.

**Bulgular:** Altmış yedi hastanın 39'u (%58,2) erkek, 28'i (%41,8) ise kadındı ve erkek/kadın oranı 3:2 idi. Erkeklerin ortalama yaşı 63,4±11,7; kadınların ise 59,3±14,3 yılı idi. Ortalama tümör boyutu erkeklerde 5,7; kadınlarda ise 5,3 cm idi. Ortalama yaş, tümör boyutu ve Fuhrman derecesinde fark saptanmasına rağmen anlamlı seviyeye ulaşmadı. Erkeklerin 24'ü düşük, 15'i yüksek; kadınların ise 25'i düşük, 3'ü yüksek evreli hastalığa sahipti. Yani erkekler istatistiksel olarak anlamlı şekilde kadınlardan daha yüksek evreli hastalığa sahipti (p=0,011).

**Sonuç:** Sonuç olarak, kadın popülasyonumuz erkekler göre anlamlı şekilde daha düşük evreli tümöre sahip olmasına rağmen, tümörlerin derecesi ve boyutları anlamlı bir farklılık göstermedi. Sonuçlarımız Avrupa çalışmalarıyla uyumlu bulundu.

**Anahtar Kelimeler:** Böbrek hücreli karsinom, Cinsiyet, Farklılık, Radikal, Nefron koruyucu, Nefrektomi

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## Introduction

Currently, kidney cancer is the ninth most common malignancy in men and 14<sup>th</sup> most common in women, it is also the 16<sup>th</sup> most common cause of death from cancer worldwide. There were an estimated 338.000 new cases and 143.000 deaths from kidney malignancies in 2012 (1). Cancers originating from renal parenchyma cells account for nearly 85 percent of the newly diagnosed kidney cancers in the United States of America. Other types of kidney cancers include renal pelvis cancer (12%) and rare malignancies (2%). Clear cell carcinoma comprises more than 70% of renal cell carcinoma (RCC) and papillary carcinoma (15%) and chromophobe carcinoma (5%) are the other main histologic types (2). The incidence of RCC has been gradually increasing in the United States of America and Europe in the past thirty years (3). Also, there is a two-fold increase in mortality and a five-fold increase in new cases of RCC when compared with 70's (4).

Despite the increasing rates, the incidence of RCC amongst genders is distinctly different. The rates were about twice as high for males than for females. However, the ratio has remained approximately same (5). Hormonal and reproductive factors which include the use of hormone therapy, oral contraceptives and parity may be the reason behind this gender-specific difference in incidence (6). Some studies indicate that men present with RCC with higher stage, larger tumors and at younger age than women (7). Most of the previous studies on gender-specific features of RCC included patients from Europe or the United States of America and there is little information about the gender-specific features of Turkish patients with RCC in the literature.

The aim of the study was to investigate gender-specific differences in the Turkish patients with RCC undergoing radical or nephron-sparing nephrectomy and compare the results with those in other regions.

## Materials and Methods

After Muğla Sıtkı Koçman University Local Ethics Committee's approval with 180085 decision number, data of 76 patients, who were clinically diagnosed with RCC and underwent radical or nephron-sparing nephrectomy in our department from January 2011 to August 2017, were retrospectively evaluated. A total of nine patients were excluded from the study because they had non-RCC pathological type tumors (5 oncocytoma, 2 fat-poor angiomyolipoma and 2 upper urothelial cell carcinoma). Therefore, 67 patients were included in the study.

In addition to the age and gender of the patients, data on the size, histological type, grade and pathological stage of the tumors were obtained. All the pathologic materials were

processed according to the standard procedures and assessed by an experienced genitourinary pathologist at our institution. The 2009 American Joint Committee on Cancer tumor-node-metastasis (TNM) staging system was used to assign pathological stages (8). The Fuhrman grading system was used for nuclear grading (9).

## Statistical Analysis

Pearson's chi-square test was used for comparing categorical variables, whereas the Student's t-test was used for the same purpose in continuous variables. Very few patients died during the study, consequently, no survival analysis could be conducted. The software Statistical Package for the Social Sciences 22.0 (SPSS Inc., Chicago, United States of America) was used to assess data. A p value of less than 0.05 was considered statistically significant.

## Results

The clinicopathological features of the patients and comparison results are shown in Table 1. Of the 67 patients; 39 (58.2%) were male and 28 (41.8%) were female; male-to-female ratio was 3:2. The mean age of the male and female patients was 63.4±11.7 years and 59.3±14.3 years, respectively and the mean tumor size was 5.7 cm and 5.3 cm, respectively. There were differences in mean age, tumor size and Fuhrman grade, however, none of them reached the level of statistical significance. Twenty four of the male and 25 of the female patients had low-stage, while 15 of the male and 3 of the female patients had high stage disease. Thus, the incidence of high stage disease in male patients was higher than in female patients and the difference was statistically significant (p=0.011). Papillary RCC was found in 3 of the male and 2 of the female patients and chromophobe RCC was detected in 1 of the males and 2 of the females. Because of the low number of cases, the histological subtypes were not included in the analysis.

## Discussion

To the extent of our knowledge, there is no study in the literature which investigates the gender-related differences in patients with RCC in the Turkish population. Although the present cohort represent only a small part of the Turkish population with RCC, it may guide the further studies with larger cohorts and be used to compare the results with the other regions of the world.

Largest studies in the literature, which were conducted with more than thirty thousand patients, have shown that the male-to-female ratio for patients with RCC was nearly 2:1. Aron et al. (10) assessed the results of 35.336 patients and found a male-to-female ratio of 7:4, while Stafford et al. (11) reached the same result with 39.434 patients. Moreover, Woldrich et al. (12) found

**Table 1. The clinicopathological features and comparison results of the patients**

Variable	Total	Male	Female	p value
Patients, n (%)	67	39 (58.2)	28 (41.8)	0.222
<b>Mean (SD)</b>				
Age (years)	61.73 (12.9)	63.4 (11.7)	59.3 (14.3)	0.200
Tumor size (cm)	5.5 (2.5)	5.7 (2.4)	5.3 (2.6)	0.465
<b>Pathological tumor stage</b>				
				0.011
T1	34	17	17	-
T2	15	7	8	-
T1+T2 (low stage)	49	24 (61.53)	25 (89.28)	-
T3	14	12	2	-
T4	4	3	1	-
T3+T4 (high stage)	18	15 (38.46)	3 (10.72)	-
<b>Fuhrman grade</b>				
				0.982
G1	6	2	4	-
G2	30	19	11	-
G1+G2 (low grade)	36	21 (53.8)	15 (53.57)	-
G3	17	9	8	-
G4	14	9	5	-
G3+G4 (high grade)	31	18 (46.15)	13 (46.42)	-

SD: Standard deviation, G: Grade

a ratio of 8:5 with more than 236.000 cases. Contrary to these studies, we found a male-to-female ratio of 3:2. In line with our study, Schrader et al. (13) from Germany and Hew et al. (14) from Netherlands demonstrated the same ratio. Although the ratio varies, the incidence of RCC is higher in males than in females. Despite the lack of evidence, some studies have suggested that hormonal and reproductive factors may explain the low incidence of RCC in women (6,15).

Most of the large population-based studies indicated that female patients were older than males at the time of diagnosis (13,14). A study by Woldrich et al. (12) including 236.930 patients showed that the mean age of females and males were 64.3 and 62.9 years, respectively. In addition, Stafford et al. (11) and Aron et al. (10) reached similar results regarding the age difference between genders. However, in a study by Lee et al. (16) performed in South Korea, there was no statistically significant difference in mean age between genders. Unlike most of the articles in the literature, in our study, the mean age of males was higher than females, but the difference did not reach the level of statistical significance. Consistent with our study, Chen et al. (17) found that compared with male patients, female patients were younger, but the difference was not significant.

There are conflicting results about difference in tumor size between genders in the publications. Some of the previous studies found no difference in the tumor size between genders (16,17,18). However, Hew et al. (14) and Aron et al. (10) found that the mean tumor size in females were smaller than in males. In accordance, we found that the mean tumor size in females was smaller, but the difference was not statistically significant. Contrary to these results, the mean tumor size in females was higher in a non-significant level, in a study by Lee et al. (16).

Because of the low number of our cases, we converted the Fuhrman grading system into low grade and high grade by merging grade 1 with 2 and grade 3 with 4, respectively. The same process was repeated for the TNM staging of the tumors. Females tend to have more low-grade tumors (10,14,17). However, we found no significant difference in tumor grade between genders in our study. Schrader et al. (13) assessed 780 patients treated with nephrectomy and found no difference in grades, in line with our study. Women present with lower stage tumors than man despite the different staging systems (10,11,12,19,20). In agreement with previous studies, we also found that female patients had lower stage tumors. Hew et al. (14) reported less common pT3 stage tumors in women,

interestingly, except in those younger than 40 years. However, May et al. (21) assessed the results of 6136 patients with RCC and reported no significant difference in tumor stage between genders. Currently there is no clear explanation for the pathological difference in RCC between genders. However, gender-specific molecular markers and hormone receptors in RCC may play a major role in clarifying this difference.

Further nationwide, multicenter studies with more detailed data collection are warranted for better understanding of the gender-related differences in Turkish patients with RCC.

### Study Limitations

The limitations of our study must be noted. In addition to its retrospective design, we could only assess patients who underwent surgery. Moreover, as a result of small sample size; neither we could conduct histologic subtype analysis nor survival analysis. We did not have sufficient data about female clinical characteristics, such as age of menopause, pregnancy or parity. Also, information about the potential risk factors, symptoms, and incidental detection rates were lacking. Such information may be useful in explaining gender-related differences.

### Conclusion

Turkish women with RCC had significantly lower stage tumors than Turkish men, although stage and size of tumor did not present a statistical significant difference. Also, the difference between mean age did not reach the significant level. Gender-related differences in patients with RCC in the Turkish population are similar with that in other regions of the world, but larger scale studies are needed.

### Ethics

**Ethics Committee Approval:** The study was approved by the Muğla Sıtkı Koçman University Local Ethics Committee with 180085 decision number.

**Informed Consent:** The study is retrospective.

**Peer-review:** Externally and internally peer-reviewed.

### Authorship Contributions

Surgical and Medical Practices: İ.A., Y.D., H.T., H.D., H.Ş., Concept: İ.A., H.Ş., Design: İ.A., H.Ş., Data Collection or Processing: İ.A., Y.D., H.T., H.D., Analysis or Interpretation: İ.A., Y.D., Literature Search: İ.A., H.T., H.D., Writing: İ.A.

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