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Clinical and histopathological characteristics of patients with renal cell cancer larger than 10 cm

10 cm'den büyük böbrek hücreli kanserli hastaların klinik ve histopatolojik özellikleri

Adem Emrah Coguplugil[1], Selahattin Bedir[1]

[1]Gülhane Training and Research Hospital, Department of Urology, Ankara, Türkiye

ABSTRACT

***Aim*:** In this study, we aimed to evaluate the clinical and histopathological characteristics of patients with renal cell cancer (RCC) > 10 cm.
Methods: Data of patients who underwent radical/partial nephrectomy due RCC were retrospectively evaluated. Patients were divided into two groups according to their tumor sizes (≤10 cm and >10 cm). The data of demographics, histological tumor subtype, tumor grade, survival after nephrectomy, and metastasis were recorded.
Results*:* Data from 116 patients were analysed. Mean age of the patients was 57.6 years. The mean tumour size was 50 (range: 15-150) mm in preoperative tomography, and 50 (range: 10-140) mm in pathology specimen. Mean follow up of time was 24.59±12.95 months. Out of 116 patients included in the study, tumour size were >10 cm in 15 patients (group 1) and ≤10 cm in 101 patients (group 2). Radical nephrectomy was performed to all patients in group 1. In group 2, 49 (48.5%) patients underwent partial nephrectomy and 52 (51.5%) patients underwent radical nephrectomy. The incidence of higher stage and higher grade in group 1 was significantly higher than group 2 ($p<0.05$). Distant metastasis was present in 3 (20%) patients from group 1 and 5 (4.9%) patients from group 2 ($p<0.05$). Cancer specific survival (CSS) was significantly higher in group 2 than in group 1 (96.1% vs. 86.6%, $p<0.05$).
Conclusion: Patients with RCC >10 cm have a higher metastasis rate and lower CSS. These patients should be followed more carefully for metastasis.

Keywords*:* grade; histologic type; metastasis; renal cell carcinoma; stage

ÖZET

Amaç: Bu çalışmada >10 cm böbrek kanseri (BK) olan hastaların klinik ve histopatolojik özelliklerini değerlendirmeyi amaçladık.
Yöntem: BK nedeniyle radikal/parsiyel nefrektomi yapılan hastaların verileri geriye dönük olarak değerlendirildi. Hastalar tümör boyutlarına göre (≤10 cm ve >10 cm) iki gruba ayrıldı. Demografik özellikler, histolojik tümör alt tipi, tümör derecesi, nefrektomi sonrası sağkalım ve metastaz verileri kaydedildi.
Bulgular: 116 hastanın verileri analiz edildi. Hastaların ortalama yaşı 57.6 idi. Ortalama tümör boyutu ameliyat öncesi tomografide 50 mm (dağılım: 15-150) mm ve patoloji örneğinde 50 mm (dağılım: 10-140) idi. Ortalama takip süresi 24.59±12.95 aydı. Çalışmaya dahil edilen 116 hastanın tümör boyutu 15 hastada >10 cm (grup 1), 101 hastada ≤10 cm (grup 2) idi. Grup 1'deki tüm hastalara radikal nefrektomi yapıldı. Grup 2'de 49 hastaya (%48.5) parsiyel nefrektomi ve 52 hastaya (%51.5) radikal nefrektomi uygulandı. Daha yüksek evre ve daha yüksek derece insidansı grup 1'de grup 2'ye göre anlamlı derecede yüksekti ($p<0.05$). Grup 1'de 3 (%20) hastada ve grup 2'de 5 (%4.9) hastada uzak metastaz mevcuttu ($p<0.05$). Kansere özgü sağkalım (KÖS), grup 2'de grup 1'e göre anlamlı olarak daha yüksekti (%96.1'e karşı %86.6, $p<0.05$).
Sonuçlar: >10 cm BK olan hastalarda metastaz oranı daha yüksek ve KÖS daha düşüktür. Bu hastalar metastaz açısından daha dikkatli takip edilmelidir.

Anahtar kelimeler*:* evre; histolojik tip; metastaz; böbrek kanseri; derece

Introduction

The use of computerized tomography (CT) and magnetic resonance imaging (MRI) has increased the detection of incidental and small renal cell carcinomas (RCC) (Dorin et al., 2014). Most of the RCC patients have no symptoms at the time of diagnosis (Mason et al., 2011). The detected RCC are generally small in size and of a lower stage. Therefore, the incidence of large RCC has decreased nowadays. Tumour size, stage (Tumour Node Metastasis [TNM]), grade, and pathological subtype provide important prognostic information (Frank et al., 2003). The most common histological subtype in adults is clear cell RCC (Moch, Cubilla, Humphrey, Reuter & Ulbright, 2016). Tumour size is very important in both RCC staging and prognosis. 7.1% of patients with tumours of 4 cm or less may present with metastatic disease (Sun, Shariat, & Karakiewicz, 2010). On the other hand, the metastasis rate in large RCC (>10 cm) is reported to be 12% (Hamidi, Süer, Gökçe, Bedük & Baltacı, 2017). In this study, we are comparing the characteristics of RCC patients surgically treated for ≤10 cm and >10 cm RCC.

Methods

Adult patients who underwent nephrectomy (open or laparoscopic, total or partial) with the diagnosis of RCC between August 2016 and December 2020 were reviewed retrospectively. Patients demographics, tumour stage, histological tumour subtype, tumour grade, postoperative survival rates, pathological and radiological size, and metastasis data were recorded. Intravenous contrast-enhanced abdomino-pelvic CT was performed to all patients preoperatively. 2017 TNM classification system was used. Fuhrman grading system was used to grade RCC (grade I-IV). Patients were divided into 2 groups according to pathological tumour size. Group 1 consisted of patients with

Corresponding Author: Adem Emrah Coguplugil, Gülhane Training and Research Hospital, Department of Urology, Ankara, Türkiye
Phone: +90 0530 380 95 24 E-mail: aemrahco@yahoo.com
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ORCID: Adem Emrah Coguplugil: 0000-0002-6240-4989, Sercan Yılmaz: 0000-0003-4999-9217

tumours larger than 10 cm. Group 2 consisted of patients with tumours 10 cm or less. Both groups were compared with regard to patient demographics, TNM stage, grade, pathological subtype, and radiological and pathological tumour sizes.

Statistical analysis was done using Statistical Package for Social Sciences 25.0 software (SPSS 25.0 for MAC). Descriptive statistics of non-continuous samples were expressed with numbers and percentiles. Shapiro- Wilk, Kurtosis, and Skewness Tests were used to assess the continuous variables' normalization. After this procedure, descriptive statistics of continuous variables without normal distribution were expressed as median (minimum - maximum), and descriptive statistics of continuous variables with normal distribution were expressed as mean ± standard deviation (minimum - maximum). Chi Square Test was used to compare the independent nominal parameters. Kaplan Meier Survival analyses was used to detect the survivals among subgroups. Probability of p <0.05 was accepted as statistically significant

Ethical aspect of the study

Health Sciences University Gülhane Faculty of Medicine Ethics Committee approved this study (Date: 25 February 2021; Number: 2021-92) Helsinki Declaration rules were followed and patient written informed consent was obtained (64th WMA General Assembly, Fortaleza, Brazil, October 2013).

Table 1. Patient characteristics

Variables	Mean, median or n (%)
Number of patients	116
Age, years	57.6 (range: 28-86)
Gender	
Male	74 (63.8%)
Female	42 (36.2%)
Tumour side	
Right	57 (49.1%)
Left	59 (50.9%)
Follow up, months	24.59 ± 12.95 (range: 2-53)
Tumour size, mm	
Radiological	50 (15-150)
Pathological	50 (10-140)
Type of surgery	
Partial nephrectomy	50 (43.1%)
Radical nephrectomy	66 (56.9%)
Histological type	
Clear cell RCC	87 (75%)
Chromophobe RCC	13 (11.2%)
Papillary RCC	12 (10.3%)
Others	4 (3.4%)
Tumour classification	
T1	70 (60.3%)
T2	11 (9.5%)
T3	29 (25%)
T4	6 (5.2%)
Fuhrman's grade	
1	7 (6%)
2	47 (40.5%)
3	37 (31.9%)
4	11 (9.5%)
Nodal involvement	5 (4.3%)
Distant metastasis	8 (6.9%)
Tumour necrosis	39 (33.6%)
Sarcomatoid component	4 (3.4%)

Results

Medical records of 116 patients were available and analysed. Patient characteristics are shown in Table 1. 74 patients were male (63.8%) and 42 patients were female (36.2%). Mean patient age at nephrectomy was 57.6 ± 12.92 (range: 28-86) years. Mean follow up time was 24.59 ± 12.95 (range: 2-53) months. 57 (49.1%) of the RCC were right sided and 59 (50.9%) were left sided. 39 (33.6%) patients underwent open partial nephrectomy (PN), 11 (9.4%) patients laparoscopic PN, 44 (37.9%) patients open radical nephrectomy (RN), and 22 (19%) patients laparoscopic RN. Histological types were as follows: 87 (75%) clear cell RCC (ccRCC), 13 (11.2%) chromophobe RCC (chRCC), 12 (10.3%) papillary RCC (pRCC), and 4 (3.4%) others. Fuhrman grades II (40.5%) and III (31.9%) were most common.

Table 2. Characteristics of patients with tumours ≤ 10 (group1) cm and > 10 cm (group 2)

Variables	Group 1 Mean or n (%)	Group 2 Mean or n (%)	p value*
Number of patients	15	101	
Age, years	55.4 (range: 33-77)	57.9 (range: 28-86)	
Gender			
Male	12 (80%)	62 (61.4%)	
Female	3 (20%)	39 (38.6%)	
Tumour side			
Right	5 (33.3%)	52 (51.5%)	
Left	10 (66.6%)	49 (48.5%)	
Tumour size, mm			
Radiological	119.2	50.6	0.01
Pathological	117.6	49.4	0.03
Type of surgery			
Partial nephrectomy	0	49 (48.5%)	0.01
Radical nephrectomy	15 (100%)	52 (51.5%)	
Histological type			
Clear cell RCC	11 (73.3%)	76 (75.3%)	
Chromophobe RCC	3 (20%)	10 (9.9%)	
Papillary RCC	0	12 (11.9%)	
Others	1 (6.6%)	3 (2.9%)	
Tumour classification	0	70 (69.3%)	
T1	4 (26.6%)	7 (6.9%)	
T2	8 (53.3%)	21 (20.7%)	0.01
T3	3 (20%)	3 (2.9%)	0.01
T4			
Fuhrman's grade			
1	0	7 (6.9%)	
2	3 (20%)	43 (42.6%)	
3	5 (33.3%)	32 (31.7%)	
4	4 (26.6%)	7 (6.9%)	0.03
CSS	86.6	96.1	0.03
Nodal involvement	3 (20%)	2 (1.9%)	0.01
Distant metastasis	3 (20%)	5 (4.9%)	0.01
Tumour necrosis	11 (73.3)	28 (27.7%)	0.01
Sarcomatoid component	0	4 (3.9%)	

RCC: Renal cell carcinomas, CSS: Cancer specific survival
* p value <0.05 statistically significant

The median tumour size was 50 (range: 15-150) mm in preoperative CT, and 50 (range: 10-140) mm in pathology specimen (p=0.073). There were 15 (12.9%) patients in group 1 and 101 (87.1%) patients in group 2 (Table 2). Mean patient age was 55.4 (range: 33-77) in group 1 and 57.9 (range: 28-86) in group 2. RN was performed to all patients in group 1. In group 2, 49 (48.5%) patients underwent PN and 52 (51.5%) patients underwent RN. The incidence of higher T stage and

higher Fuhrman grade in group 1 was significantly higher than group 2 (p<0.05). Distant metastasis was present in 3 (20%) patients from group 1 and 5 (4.9%) patients from group 2 (p<0.05). Lymph node involvement was present in 3 (20%) patients from group 1 and 2 (1.9%) patients from group 2 (p<0.05). 2 patients in group 1 and 4 patients in group 2 died due to RCC during follow-up. Overall survival was 93.2% in group 2 and 86.6% in group 1. Cancer specific survival (CSS) was significantly higher in group 2 than in group 1 (96.1% vs. 86.6%, p<0.05). Metastatic patients had poorer survival in both groups.

Discussion

Various prognostic factors associated with the patient and the tumour have been described in RCC. The most important prognostic factors related to the tumour are stage, size, Fuhrman grade, and histological subtype.

RCC size is one of the most important component of TNM staging and also it remains one of the most important prognostic factors. Waalkes et al. (2011) reviewed the data of 445 patients with RCC 7-10 cm and 134 patients with RCC >10 cm. The authors reported that there was no significant difference in CSS between these groups (Waalkes et al., 2011). In another study, Hamidi et al. (2017) retrospectively reviewed the data of 120 patients with RCC <10 cm and 116 patients with RCC >10 cm and found that CSS was significantly higher in patients with RCC < 10 cm. The authors reported that the metastasis rate for RCC >10 cm was 12% (Hamidi et al., 2017). Frank et al. (2005) evaluated 544 patients and reported that the patients with RCC >10 cm had a worse prognosis than those with 7-10 cm RCC. In our study, we found that tumour stage and grade was higher and CSS was lower in patients with RCC >10 cm. Also, distant metastasis rate was higher in patients with RCC >10 cm compared to patients with RCC ≤10 cm.

Additionally, tumour size is the most important factor in determining the eligible patients for partial nephrectomy. PN is strongly recommended to patients with T1 RCC. If technically feasible, PN should be performed in patients with T2 RCC and a solitary kidney or chronic kidney disease (Ljungberg et al., 2021). There are several reports comparing radiological and pathological RCC size. Lee et al. (2010) investigated the difference between tumour sizes measured via preoperative contrast-enhanced CT images and surgical specimens during pathological examinations in 467 patients who underwent partial or radical nephrectomy for RCC. They found that the mean radiographic tumour size was insignificantly larger than the pathologic tumour size (Lee et al., 2010). In a retrospective study by Yaycioglu Rutman, Balasubramaniam, Peters and Gonzalez (2002) 291 open nephrectomy patients treated for non-metastatic RCC were evaluated for tumour size. The authors reported no significant difference between average radiologic tumour size (measured by contrast-enhanced CT) and pathologic tumour size. In our study, the median radiologic tumour size was larger than pathologic tumour size in both RCC ≤10 cm and RCC >10 cm but the difference was not significant.

Fuhrman grade represents one of the foremost prognostic variables in patients with RCC. Higher Fuhrman grade is associated with higher mortality rates. In a retrospective study with a large patient population (n=14 064), Sun et al. (2009) reported that cancer specific mortality rates were 6.7%, 13.2%, 34.4%, and 58.3% for Fuhrman grade I, II, III, and IV, respectively. They also found that the most common Fuhrman grade were II (49.9%) and III (22.4%) (Sun et al., 2009). Similarly, we found that the most common Fuhrman grades were II and III. We also found that Fuhrman grade IV was more common in patients with RCC >10 cm. Mortality rate was higher in patients with Fuhrman grade IV RCC.

RCC subtype is regarded as another important prognostic factor. But there is controversy about the effect of histological subtypes on clinical outcomes (Delahunt, Bethwaite & Nacey, 2007). Cheville, Blute, Zincke, Lohse and Weaver (2002) reported that ccRCC has a poorer prognosis compared to pRCC and chRCC. Leibovich et al. (2010) examined cancer specific death and the relationship between RCC subtype and metastasis in 3062 patients treated surgically for RCC. The authors showed significant difference in metastasis-free and CSS between patients with ccRCC and the 2 other types (pRCC and chRCC) (Leibovich et al., 2010). On the other hand, Karakiewicz et al. (2007) investigated 2530 patients in a multicenter study and found no association between histological subtype and clinical outcome. Patard et al. (2005) reported that after adjusting for TNM stage, grade and performance status, histological subtype was no longer significantly associated with survival. In our study, 4 of 6 patients who died of RCC had clear cell RCC and the mortality rate seems to be higher in clear cell RCC.

Low patient number, retrospective design and short follow up period are the main limitations of the study.

Conclusion

The actual size of RCC can be generally overestimated by CT images, but the difference is insignificant between radiologic and pathologic measurement. Stage, grade, and metastasis rates are higher and CSS is lower in patients with RCC > 10 cm. These patients should be followed more carefully for metastasis.

Conflict of Interest

The authors have no conflicts of interest to declare.

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Ethics Committee Approval

Health Sciences University Gülhane Faculty of Medicine Ethics Committee approved this study (No: 2021-92, Date: 25 February 2021).

Informed Consent

Patient written informed consent was obtained preoperatively.

Peer-review

Externally peer-reviewed.

Author Contributions

A.E.C.: Data Collection, Literature Review and Writing
S.B.: Design and İnterpretation of Data

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