ORİJİNAL ARAŞTIRMA ORIGINAL RESEARCH

DOI: 10.5336/urology.2019-70949

Survival Outcomes in Elderly Patients with Renal Cell Carcinoma: A Single-Center Experience

Renal Hücreli Karsinomlu Yaşlı Hastalarda Sağkalım Sonuçları: Tek Merkez Deneyimi

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Received: 02 Aug 2019
Accepted: 30 Sep 2019
Available online: 07 Oct 2019

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ABSTRACT Objective: The aim of the study was to investigate the survival outcomes in elderly patients with renal cell carcinoma (RCC) in our series. **Materials and Methods**: From January 2010 to June 2019, 174 patients with renal cell carcinoma who underwent surgery in our institution were analyzed. Age, gender, history, presentation, tumor size,tumor, node, metastasis (TNM) stage, histologic subtype and Fuhrman grade of the patients were recorded. Patients were divided into two groups with the cut off value 70 of age. Group 1 was defined as the patients below the 70 years of age, whereas, Group 2 was defined as the patients 70 years of age and older. **Results:** One hundred three patients were in Group 1 and 71 patients were in Group 2. Mean disease-specific survival(DSS) time was 140.3±6.7 months in Group 1, while it was 105.3±7.9 months in Group 2 (p=0.061). Mean overall survival time (OAS) was 132.0±7.5 months in Group 1 and 95.2±8.3 months in Group 2 (p=0.046). Actuarial estimated disease-specific survival at 5 years was 88.5% in Group 1and 78.1 % in Group 2 (p=0.061). Actuarial estimated overall survival at 5 years was 83.0% in Group 1 and 70.7 % in Group 2 (p=0.046). In multivariate Cox regression analysis, T stage and Fuhrman grade were independent prognostic factors for survival. **Conclusion:** Our study demonstrated that there was no statistically significant difference in disease-specific survival rates between elderly patients with RCC, those compared with younger ones. Our findings recommend that surgery may be an option for older patients with RCC to avoid the potential hazard.

Keywords: Age factor; elderly; kidney; renal cell carcinoma; survival

ÖZET Amaç: Çalışmanın amacı, serimizdeki renal hücreli karsinomlu (RHK) yaşlı hastalarda sağkalım sonuçlarını araştırmaktı. **Gereç ve Yöntemler:** Ocak 2010-Haziran 2019 tarihleri arasında kurumumuzda cerrahi uygulanan 174 renal hücre karsinomlu hasta analiz edildi. Hastaların yaş, cinsiyet, öykü, prezentasyon, tümör büyüklüğü, tümör, nodül, metastaz (TNM) evresi, histolojik alt tip ve Fuhrman derecesi kaydedildi. Hastalar eşik değeri 70 yaş olan iki gruba ayrıldı. Grup 1, 70 yaşın altındaki hastalar olarak tanımlanırken, Grup 2, 70 yaş ve üstü hastalar olarak tanımlandı. **Bulgular:** Yüz üç hasta Grup 1'de ve 71 hasta Grup 2'de idi. Grup 1'in ortalama yaşı 56,9±10,2 ve Grup 2'nin ise 77,0±5,2 idi (p <0,001). Gruplar arasında cinsiyet dağılımı açısından istatistiksel olarak anlamlı fark yoktu (p=0,643). Ortalama hastalığa özgü sağkalım (HÖS) süresi Grup 1'de 140,3±6,7 ay iken Grup 2'de 105,3±7,9 ay idi (p=0,061). Ortalama genel sağkalım (GS) süresi Grup 1'de 132,0±7,5 ay ve Grup 2'de 95,2±8,3 ay idi (p=0,046). Beş yıllık hastalığa özgü sağkalım oranı Grup 1'de %88,5, Grup 2'de% 78.1 idi (p=0.061). 5 yıllık genel sağkalım oranı, Grup 1'de %83'0, Grup 2'de %70,7 idi (p=0,046). Çok değişkenli Cox regresyon analizinde, T evresi ve Fuhrman derecesi sağkalım için bağımsız prognostik faktörlerdi. **Sonuç:** Çalışmamız, RHK'lu yaşlı hastalar arasında, genç olanlarla karşılaştırıldığında, hastalığa özgü sağkalım oranları açısından istatistiksel olarak anlamlı bir fark olmadığını göstermiştir. Bulgularımız, ameliyatın potansiyel tehlikeyi önlemek için RHK'lu yaşlı hastalar için bir seçenek olabileceğini önermektedir.

Anahtar Kelimeler: Yaş faktörleri; yaşlı; böbrek; renal hücreli kanser; sağkalım

Renal cell carsinoma (RCC) accounts for 2-3% of adult cancers and most frequently seen between 50 and 70 of ages.[1] Five percent of patients with RCC have been diagnosed below 40 years of age.[2,3] Owing to developed radiological diagnostic tools, the incidence of RCC has increased in recent years.[4-6] The average life expectancies for both men and women have been increasing worldwide.[7] Similarly with the world popu-

lation, the Turkey population is getting older. According to the World Health Organization (WHO) Turkey report, the average life expectancy is 73 (male) and 79 (female) years, and expected to increase in the future.[8] Consequently, the increased proportion of elderly patients with incidentally diagnosed kidney tumors may be a management and treatment challange in the future.

The tumor, node, metastasis (TNM) staging system, Fuhrman grade, histological subtype, and performance status are crucial factors that affect the survival of RCC.[9] Age may be one of these factors that affect prognosis of RCC. Various studies have investigated the relationship between age and survival in RCC.[2,3,10] However, the prognostic significance of the age factor is still controversial.

The present study aims to investigate the outcomes of survival in elderly individuals with RCC in our series.

MATERIAL AND METHODS

STUDY POPULATION

From January 2010 to June 2019, 174 patients with RCC who underwent surgery in our institution were analyzed. The Ethics Committee of the institution approved the study to the provisions of the Declaration of Helsinki (T.C Health Sciences University Okmeydanı Training and Research Hospital, Date: 13.04.2018, Number: 48670771- 514.10/873). Age, gender, history, presentation, tumour size, TNM stage, histological subtype, and Fuhrman grade were collected from patients records. Staging were done according to the AJCC.[11] Afterward, patients were separated into two groups with the cut off value of 70. Below the 70 years of age was defined as Group 1, whereas, the patients above the 70 years of age was defined as Group 2. The time from the surgery to death from RCC was defined as overall survival (OAS) time. The time from the surgery to death from RCC was defined as disease-specific survival (DSS) time. The tumors except from RCC were excluded from the study.

STATISTICAL ANALYSIS

The data were analyzed with SPSS version 22.0™ (IBM Corporation, California). The Kolmogorov–Smirnov test was used to test the normal distribution of the variables. The univariate analyses were performed utilizing the Mann–Whitney U test. Kaplan-Meier curves and Cox regression analyses were utilized to collate the survival rates. Statistically insignificant variables were excluded in the multivariate analysis. All p values were two-tailed. A p-value of <0.05 was noted statistically significant.

RESULTS

A total of 174 patients were evaluated. Characteristics of all patients were demonstrated in Table 1. One hundred three patients were in first Group and 71 patients were in second Group. The mean age of Group 1 was 56.9±10.2 and Group 2 was 77.0±5.2 (p<0.001). There was no statistically significant difference between gender in two groups (p=0.643). The mean tumor size was 7.1±3.0 cm in the first Group and 7.5±2.8 cm in the second Group (p=0.434). In Group 1, radical nephrectomy was performed to 61 patients and partial nephrectomy was performed to 42 patients. Forty-nine radical nephrectomies and twenty-two partial nephrectomies were performed in Group 2. In Group 1,48 patients (46.6%) were in pT1 stage, 26 patients (25.2%) were in pT2, 27 patients (26.2%) were in pT3, 2 patients (1.9%) were in pT4 stage. In Group 2, 16 patients (22.5%) were in pT1 stage, 29 patients (40.8%) were in pT2, 26 patients (36.6%) were in pT3. There was no pT4 stage patient in Group 2. Elderly patients were more likely to have high stage (pT2-pT3) tumor (p=0.005). There was no statistically significant difference in the distribution of Fuhrman grade between groups (p=0.897).

Mean disease-specific survival time was 140.3±6.7 months in Group 1, while it was 105.3 ± 7.9 months in Group 2 (p=0.061). Mean overall survival time was 132.0±7.5 months in Group 1 and 95.2±8.3 months in Group 2 (p=0.046). Actuarial estimated disease-specific survival at 5 years was 88.5 % in Group 1 and 78.1% in Group 2 (p=0.061, Figure 1). Actuarial estimated overall survival at 5 years was 83.0% in Group 1 and 70.7% in Group 2 (p=0.046, Figure 2). Table 2 presents the Cox regression analysis results. pT stage and Fuhrman

TABLE 1: Charecteristics of patients.

	Group 1 (n=103) Mean±S.D. (n%)	Group 2 (n=71) Mean±S.D. (n%)	p value
Age	56.9±10.2	77.0±5.2	***0.000***
Tumor size	7.1±3.0	7.5±2.8	0.434
Sex Male	57 (55.3%)	42(59.2%)	0.643
Female	46 (44.7%)	29(40.8%)	
Symptoms at presentation	78 (57.4%)	58 (42.6%)	0.228
Pathological stage			***0.005***
T1	48 (46.6%)	16 (22.5%)	
T2	26 (25.2%)	29 (40.8%)	
T3	27 (26.2%)	26 (36.6%)	
T4	2 (1.9%)	0 (0.0%)	
Histology			0.251
Clear cell	82 (79.6%)	52 (73.2%)	
Chromofob	6 (5.8%)	8 (11.3%)	
Sarcomatoid	6 (5.8%)	3 (4.2%)	
Papiller	4 (3.9%)	5 (7.0%)	
Ductal carsinom	0 (0.0%)	2 (2.8%)	
Others	5 (4.8%)	1 (1.4%)	
Grade			0.897
1	13 (13.5%)	6 (9.5%)	
2	43 (44.8%)	29 (46.0%)	
3	27 (28.1%)	19 (30.2%)	
4	13 (13.5%)	9 (14.3%)	
Operation type			0.204
Radical nephrectomy	61 (59.2%)	49 (69.0%)	
Parsiyel nephrectomy	42 (40.8%)	22 (31.0%)	

grade were independent predictors of survival in multivariate Cox regression analysis.

DISCUSSION

Elderly population diagnosed with renal cell carsinoma has remarkably raised in the recent years. Various studies have investigated the correlation between age and survival rates.[7,12-15] However, there are still controversial issues amongst urologists regarding to this relationship. This inconsistency could arise from different classifications of age in different studies. Our study showed that there was no significant difference on DSS rates between two groups (p=0.061). However, there was a difference in OAS rates against elderly patients (p=0.046).

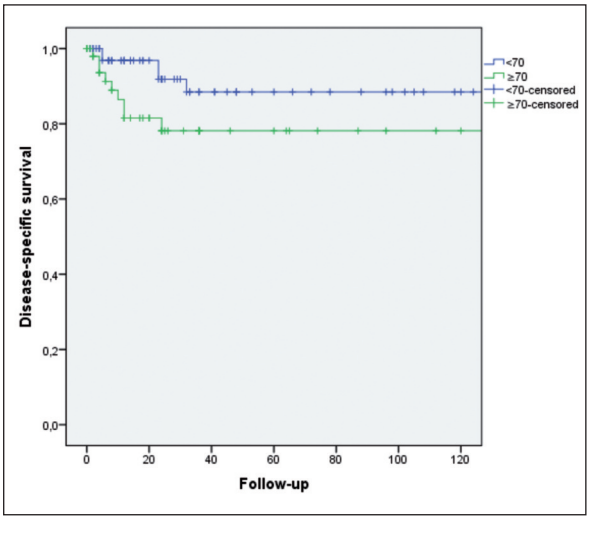

FIGURE 1: Kaplan-Meier curve demonstrating disease-specific survival in patients stratified by age.

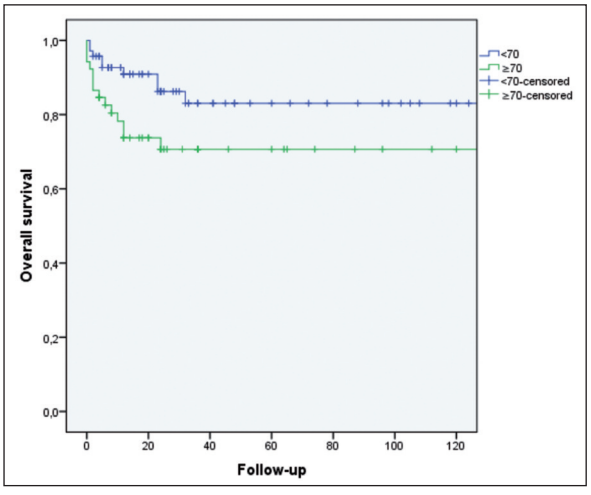

FIGURE 2: Kaplan-Meier curve demonstrating overall survival in patients stratified by age.

Our findings are compatible with previous studies. Gao et al.[14] found that older patients have significantly poorer OAS rates than those under 40 years of age. However, they have not found the statistically difference with regard to CSS between these groups on multivariate analysis.[14] Thompson et al. conducted a study which allocated the patients as follows (<40 years, 40-59 years, and 60-79 years) and they did not show any statistical difference in disease-specific survival rates in these groups.[12] Our study showed that elderly patients were more likely to have high stage (pT2-pT3) tumor (p=0.005). Aziz et al. reported that younger individuals had a more local disease, more chromophobe histologic type, smaller cancer diameters, and desirable disease-specific survival rates.[10] Taccoen et al. demonstrated that Renal cell carsinoma in younger adults was generally local at initial and had a better prognosis than elderly individuals.[2] In a study from Turkey, Yıkılmaz et al. divided the patients into two groups according to age as follows ≤50 years and >50 years.[16] They reported that there was no significant difference regarding to gender, tumor size, laterality, surgical and pathologic features between two groups.[16]

The TNM stage is a broadly utilized prognostic factor for cancer survival.[17] Şimşek et al. reported that radiological lymph node involvement and stage were independent predictors that affecting the survival rates of renal cell carsinoma patients.[18] Low TNM stage tumors are associated with better survival rates.[19] In our study, the younger group had a lower pT stage. Additionally, in Cox regression analysis, pT stage and Fuhrman grade were independent predictors for survival. We think that this result may arise from the increased early detection of renal masses. Patients with incidentally diagnosed renal masses incline to demonstrate with a lower grade and stage. Also they seem to have better desirable survivals than those with symptomatic patients.[13,20,21]

In this study, there was no statistically significant difference in the distribution of Fuhrman grade between groups (p=0.897). Our findings regarding the distribution of histological subtypes are compatible with previous reports. Chromophobe, pa pillary and clear cell, histology account for about 5%, 10% and 80% of all renal cell carcinomas, respectively.[22] Kim et al. found that chromophobe histology was dominant in younger patients in their study.[13] In

TABLE 2: Univariate and multivariate Cox regression analysis results.

	Univariate analysis	Multivariate analysis	
Variable	*p*	HR (95% CI)	*p*
Age	0.074	2.71 (0.90-8.09)	
Gender	0.760	1.17 (0.40-3.38)	
Symptomatic	0.200	30.7 (0.16-583.2)	
Stage	**<0.001**	18.7 (4.87–73.11)	**<0.001**
Fuhrman grade	**<0.001**	5.69 (1.29–16.21)	**<0.001**
Histology	0.350	0.63 (0.21–1.65)	

general, chromophobe subtype has a lower progression risk compared with other histologic subtypes.[23] Another study showed that histology of clear cell rises with age, whereas histology of chromophobe reduces with age.[3] One study reported that the histology of clear cell reduces with growing decade of life whereas the histology of papillary rises with the growing decade, and the histology of chromophobe does not alter with the decade.[24]

Guidelines currently promote surgical approach for resectable renal masses.[7] Other treatment options are ablation or expectant management (EM) which has become known management strategy, especially in small renal masses.[25-27] Expectant management has attracted the attention, especially, the management of elderly individuals with a limited life expectancy with its advantages such as modest annual growth rates, low metastatic potential, and low risk of cancer-related mortality.[7]

Life expectancy and functional status are important factors for the selection of candidates for surgery. Özcan et al., in a review, concluded that the ideal treatment for renal masses in elderly individuals should be determined based on the evaluation of criteria such as comorbidities, patient age, renal function, and tumor characteristics.[28] With respect to the WHO Turkey report, the average life expectancy is 73 (male) and 79 (female) years, and expected to increase in the future.[8] Briefly, we think that only age should not be taken into account in predicting the prognosis of RCC patients after surgery. Our results recommend that surgery may be an option for older patients with RCC to avoid the potential hazard. Similar with RCC surgery, a recent study from Turkey found that oncological outcomes of radical cystectomy were comparable between young and elderly patients (cut-off value 70 years of age) and age should not constitute a contraindication for radical cystectomy operations.[29]

The first limitation of the current study is being a single-center experience and its retrospective design. Secondly, the sample size of the groups is relatively small. Another limitation of our study is no evaluation of performance status and comorbidity indices. However, despite these limitations, we consider that our results may provide sufficient contribution to the litera ture.

CONCLUSION

Consequently, our findings demonstrated no statistically significant difference in disease-specific survival rates between elderly individuals with RCC, those compared with younger ones. This study recommends that surgery may be an option for older patients with RCC to avoid the potential hazard, and only age should not be taken into account in predicting the prognosis of RCC patients after surgery.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Sait Özbir, Halil Lütfi Canat, Hasan Anıl Atalay;* ***Design:*** *Sait Özbir, Alper Ötünçtemur, Fatih Altunrende;* ***Control/Supervision:*** *Fatih Altunrende, Alper Ötünçtemur, İlter Alkan;* ***Data Collection and/or Processing:*** *Erdal Abay, İlter Alkan, Sait Özbir;* ***Analysis and/or Interpretation:*** *Sait Özbir, Alper Ötünçtemur, İlter Alkan;* ***Literature Review:*** *Sait Özbir, Fatih Altunrende, Hasan Anıl Atalay;* ***Writing the Article:*** *Sait Özbir;* ***Critical Review:*** *Alper Ötünçtemur, İlter Alkan, Fatih Altunrende, Halil Lütfi Canat.*

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