ORIGINAL ARTICLE

DOI: 10.4274/nkmj.galenos.2024.75010
Nam Kem Med J 2024;12(3):217-224

Prognostic Factors and Treatment Outcomes in Renal Cell Carcinoma: A Comprehensive Analysis

Renal Hücreli Karsinomda Prognostik Faktörler ve Tedavi Sonuçları: Kapsamlı Bir Analiz

Ömer Faruk ELÇİÇEK, Mehmet KÜÇÜKÖNER

Dicle University Faculty of Medicine, Department of Medical Oncology, Diyarbakir, Turkey

ABSTRACT

Aim: We aimed to investigate the prognostic factors, factors affecting survival and the prognostic value of the Memorial Sloan-Kettering Cancer Centre (MSKCC) risk score in renal cell carcinoma (RCC) patients. In addition, we assessed the survival and potential adverse effects of sunitinib and pazopanib tyrosine kinase inhibitors.

Materials and Methods: The study included patients diagnosed with RCC aged ≥18 years, who were followed up in our clinic between 2006 and 2020. The clinicopathological characteristics were recorded in the hospital's electronic data system. In the entire patient population, survival and prognostic factors were investigated. Furthermore, prognostic factors in terms of treatment (pazopanib vs. sunitinib) for advanced stage patients were evaluated as well.

Results: Two hundred and two patients were included in this study. Fifty-five of the patients were female, 147 patients were male. Most common histological type was clear cell carcinoma (59%). At the time of presentation, 57% of the patients were in the early stage (stage 1,2,3). The median overall survival (mOS) was 16.8 months in stage 4 patients and 82.5 months in early stage patients. mOS was 69.1 months in the favorable MSKCC risk group while it was 6.8 months in the poor risk group. In the sunitinib arm, the median progression-free survival (mPFS) was 11.1 months, and mOS was 18.1 months. In the pazopanib arm, mPFS was 12.2 months, and mOS was 17.4 months. There was no significant difference in response rate, mPFS, and mOS between the two drugs.

Conclusion: In this study, we have shown that risk and performance scorings with some laboratory and clinical evaluations, which are still cheap and easily accessible, are valuable and usable in showing prognosis in RCC patients. Disease stage, MSKCC risk score, Eastern Cooperative Oncology Group, and Karnofsky performance scores showed prognostic characteristics in RCC. There was no survival difference between histological subtypes. The efficacy of sunitinib and pazopanib in metastatic first-line treatment was similar, but pazopanib was superior in terms of any grade adverse events.

Keywords: Renal cell carcinoma, RCC, MSKCC score, sunitinib, pazopanib

ÖZ

Amaç: Renal hücreli karsinom (RCC) hastalarında prognostik faktörleri, sağkalımı etkileyen faktörleri ve Memorial Sloan-Kettering Kanser Merkezi (MSKCC) risk skorunun prognostik değerini araştırmayı amaçladık. Ayrıca, tirozin kinaz inhibitörleri olarak sunitinib ve pazopanibin sağkalım sonuçlarını ve yan etkilerini değerlendirdik.

Gereç ve Yöntem: Çalışmaya 2006-2020 yılları arasında kliniğimizde takip edilen ≥18 yaş RCC tanılı hastalar dahil edilmiş olup, klinikopatolojik özellikler hastanenin elektronik veri sistemine kaydedilmiştir. Tüm hasta popülasyonunda sağkalım ve prognostik faktörler araştırılmış, ayrıca ileri evre hastalar için tedavi (pazopanib vs. sunitinib) açısından prognostik faktörler de değerlendirilmiştir.

Bulgular: Bu çalışmaya 202 hasta dahil edildi. Hastaların 55'i kadın 147'si erkekti. En sık görülen histolojik tip berrak hücreli karsinomdu (%59). Başvuru sırasında hastaların %57'si erken evredeydi (evre 1,2,3). Dördüncü evre hastalarda ortanca genel sağkalım (mOS) 16,8 ay iken, erken evre hastalarda mOS 82,5 aydı. mOS, MSKCC iyi risk grubunda 69,1 ay iken, kötü risk grubunda 6,8 aydı. Sunitinib kolunda medyan progresyonsuz sağkalım (mPFS) 11,1 ay ve mOS 18,1 ay, pazopanib kolunda ise mPFS 12,2 ay ve mOS 17,4 aydı. İki ilaç arasında yanıt oranı, mPFS ve mOS açısından anlamlı bir fark bulunamadı.

Address for Correspondence: Ömer Faruk ELÇİÇEK MD, Dicle University Faculty of Medicine, Department of Medical Oncology, Diyarbakir, Turkey
Phone: +90 532 486 30 21 **E-mail:** omerfarukelcicek@gmail.com **ORCID ID:** orcid.org/0000-0002-2919-8132
Received: 22.05.2024 **Accepted**: 09.07.2024

Sonuç: Bu çalışmada, halen ucuz ve kolay erişilebilir olan bazı laboratuvar ile klinik değerlendirmelerle birlikte yapılan risk ve performans skorlamalarının RCC hastalarında prognozu göstermede değerli ve kullanılabilir olduğunu gösterdik. Hastalık evresi, MSKCC risk skoru, Eastern Cooperative Oncology Group ve Karnofsky performans skorları RCC'de prognostik özellik gösterdi. Berrak hücreli ve diğer histolojik alt tipleri arasında sağkalım farkı bulunmadı. Metastatik hastalıkta birinci basamak tedavide sunitinib ve pazopanib tiroin kinaz inhibitörlerinin etkinliği benzer bulundu, ancak pazopanib yan etki açısından daha üstündü.

Anahtar Kelimeler: Renal hücreli karsinom, RCC, MSKCC skoru, sunitinib, pazopanib

INTRODUCTION

Renal cell carcinoma (RCC) is the most common kidney cancer in adults and is a renal parenchymal cancer of the adenocarcinoma cell type. It accounts for approximately 4% of adult malignancies and more than 90% of neoplasms arising from the kidneys[1]. According to globocan 2022 data, approximately 435,000 new cases and 156,000 deaths were reported worldwide annually[1]. Although the incidence is increasing, mortality is decreasing due to new treatments[2] .

RCC is characterized by several subtypes with distinct genetic and molecular profiles. Clear cell (~70%), papillary (~15%), chromophobe (~5%), oncocytic (~5%), and collecting duct (Bellini) origin (<1%) subtypes exist[3]. Sarcomatoid differentiation is not a separate histological subtype and may be observed together with other RCC subtypes[4]. These tumors have a more aggressive prognosis, and approximately 75% of the patients were metastatic at the time of diagnosis[5]. Many RCCs are diagnosed when local invasion or metastasis occurs. In addition, recurrence may develop in patients who are initially resectable and undergo surgery, and systemic treatment (targeted agents, immunotherapy, radiotherapy) may be required. Systemic treatment is initiated immediately in metastatic or locally advanced disease. In localized disease, surgical resection is the most effective and curative treatment method. RCC is resistant to most chemotherapeutic agents due to the expression of the multidrug resistance protein P-glycoprotein, which originates from the proximal tubule. In recent years, targeted therapies have come to the forefront in RCC with a better understanding of molecular mechanisms[6].

Overall, the management of RCC has evolved significantly with the introduction of targeted therapies and immunotherapies. Ongoing research continues to unravel the complex biology of RCC, aiming to improve patient outcomes through personalized and combination therapies [7-9].

In this study, we aimed to investigate the predictive factors for recurrence and survival in patients with RCC and to evaluate the efficacy and adverse effects of tyrosine kinase agents.

MATERIALS AND METHODS

For our study, permission was obtained from the Dicle University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee with decision number 25 dated 05.03.2020. Between the years of 2006 and 2020, 202 patients over the age of 18 years, who were diagnosed with RCC and followed up in the Medical Oncology Clinic of Dicle University Faculty of Medicine, were included in the study. Tumors of urothelial epithelial origin were not included. Their files, demographic and clinical characteristics were analyzed. Prognostic factors related to the case and treatment were investigated, and survival analyses were performed. The histopathological type and stage of the tumor, type of surgery performed, time and sites of recurrence and metastasis were examined. Patients were grouped according to the Memorial Sloan-Kettering Cancer Centre (MSKCC) risk scores. The Karnofsky performance status (KPS) and Eastern Cooperative Oncology Group Performance Status Scale (ECOG PS) were used to evaluate the performance status of the patients. In addition, treatment effects, side effects and survival analyses were evaluated in patients receiving sunitinib and pazopanib, two tyrosine kinase inhibitors (TKI).

Overall survival (OS) was defined as the time from the date of disease diagnosis until death or the date of the last follow-up and disease-free survival (DFS) as the time from cure in early stage (stage 1, 2, 3) patients until relapse. Progression-free survival (PFS) was defined as the time from the start of treatment until disease progression or the date when it was decided that the response obtained with treatment was inadequate and the treatment approach should be changed. Treatment response was evaluated as complete response (CR), partial response (PR), srogressive disease (PD), and stable disease (SD) according to the new response evaluation criteria in solid tumors (RECIST 1.1).

Statistical Analysis

Statistical analyses of the results obtained in the study were performed using the IBM SPSS Statistics version 27 statistical software package. Descriptive statistics for continuous variables were expressed as median value, minimum and maximum value, 95% confidence interval, mean ± standard deviation, while categorical variables were expressed as number and percentage. The chi-square test was used to analyze categorical variables. Overall survival, intragroup survival, DFS and PFS were analyzed by the Kaplan-Meier test. In these tests, a p value less than 0.05 was considered statistically significant.

RESULTS

In our study, we analyzed the data from a total of 202 patients diagnosed with RCC, including 55 females (27.2%) and 147 males (72.8%). The median age of the patients was 57 years. The most common histological subtype was clear cell carcinoma, with 119 patients (59%). Forty-eight patients (23.8%) were stage 1, 33 patients (16.3%) were stage 2, 34 patients (16.8%) were stage 3, and 86 patients (43%) were stage 4. Seventy-nine patients (39%) were metastatic, and the most common sites of metastasis were the lymph nodes (62.2%) and lungs (58.7%). According to the Karnofsky score, 157 patients (78.1%) had a score greater than 80%. There were 80 patients (39.6%) with ECOG 0. According to MSKCC criteria, 66 patients (32.8%) were in the good risk group, 93 patients (46.3%) were in the intermediate risk group, and 42 patients (20.9%) were in the poor risk group. Nephrectomy was performed in 155 patients (77.1%). Clinicopathological characteristics of the patients are presented in Table 1.

In the survival analysis of the patients, we divided the early-stage patients and stage 4 patients into two separate groups for evaluation.

Results of Early Stage Patients

In this group of 115 patients, 37 were female and 78 were male. Survival was analyzed for 114 patients. Forty-seven patients (41.2%) were stage 1, 32 patients (28.1%) were stage 2, and

Table 1. Patient characteristics

Age (years), median (range)	**57 (21-83)**		
Subgroup	**n (%)**	**Subgroup**	**n (%)**
Sex		**MSKCC criteria**	
Female	55 (27.2)	Favorable	66 (32.8)
Male	147 (72.8)	Intermediate	93 (46.3)
		Poor	42 (20.9)
Histologic type		**ECOG PS**	
Clear cell	119 (59)	0	80 (39.6)
Papillary	39 (19.3)	1	81 (40.1)
Kromofob	15 (0.4)	2	21 (10.4)
Sarcomatoid	8 (3.9)	3	20 (9.9)
Other	21 (10.4)		
Stage		**Nephrectomy**	
1	48 (23.8)	Yes	155 (76.7)
2	33 (16.3)	No	47 (23.3)
3	34 (16.8)		
4	86 (43.1)		
T grade		**Nephrectomy type**	
T1	56 (28)	Partial	18 (%11.6)
T2	48 (24)	Total	137 (88.4)
T3	56 (28)		
T4	40 (20)		
N category		**Primary metastatic disease**	
N0	129 (64)	No	123 (61)
N1	70 (35)	Yes	79 (39)
Nx	3 (1)		
		Metastasis region	
		Lymph node	89 (62.2)
		Lung	84 (58.7)
Karnofsky score		Bone	62 (43.4)
<80%	45 (22)	Adrenal	26 (18.2)
≥80%	157 (78)	Liver	25 (17.5)
		CNS	13 (9.1)
		Local	11 (7.7)
		Thyroid	1 (0.7)

MSKCC: Memorial Sloan-Kettering Cancer Centre risk scores, ECOG PS: Eastern Cooperative Oncology Group Performance Status Scale, CNS: Central nervous system

35 patients (30.7%) were stage 3. The number of patients with recurrence/metastasis was 56 (49.1%). There was no gender difference in the recurrence rate. DFS and OS analyses were performed. The median DFS (mDFS) was 47.5 months and the median OS (mOS) was 82.5 months according to the time to recurrence and/or metastasis. There was no significant difference between genders in terms of DFS and OS. In stage 1 patients, mDFS was 79.2 months and mOS was 131.3 months, while in stage 3 patients, mDFS was 29.6 months and mOS was 50.3 months. mDFS and mOS durations were found to be significantly shorter as the stage progressed (mDFS p=0.001, mOS p=0.002). In patients with ECOG 0, mDFS was 72.8 months and mOS was 105 months, while in patients with ECOG 2, mDFS was 13.3 months and mOS was 78.7 months. mDFS and mOS were significantly shorter as ECOG performance score increased (mDFS p=0.001, mOS p=0.020). In the clear cell subtype, mDFS was 47.5 months and mOS was 68.3 months. In patients with non-clear cell subtype, mDFS was 59.1 months and mOS was 135.7 months. In patients with clear cells, mDFS and mOS were shorter, which was not statistically significant (mDFS p=0.327, mOS p=0.147). Survival analyses of early stage patients are shown in Table 2.

Results of Stage 4 Patients

The data of 86 patients with stage 4 RCC, including 17 female and 69 males, were analyzed. The mOS was 16.8 months in stage 4 patients. This duration was 17.7 months in men and 9.9 months in women, which was shorter in women and statistically significant (p=0.049). The duration of mOS was 17.4 months in the clear cell subtype and 16.8 months in the non-clear cell subtype, with no statistical difference (p=0.564) (Figure 1).

When survival was analysed according to the MSKCC risk assessment score, the mOS was 69.1 months in the favorable risk group, 11.1 months in the intermediate risk group, and 6.8 months in the poor risk group. According to the MSKCC risk score, survival was shorter and statistically significant as the risk status worsened (p<0.001) (Figure 2).

mOS was 32.9 months in patients with a Karnofsky score >80% and 6.8 months in patients with a Karnofsky score <80%. It was significantly shorter (p<0.001), as shown in Figure 3.

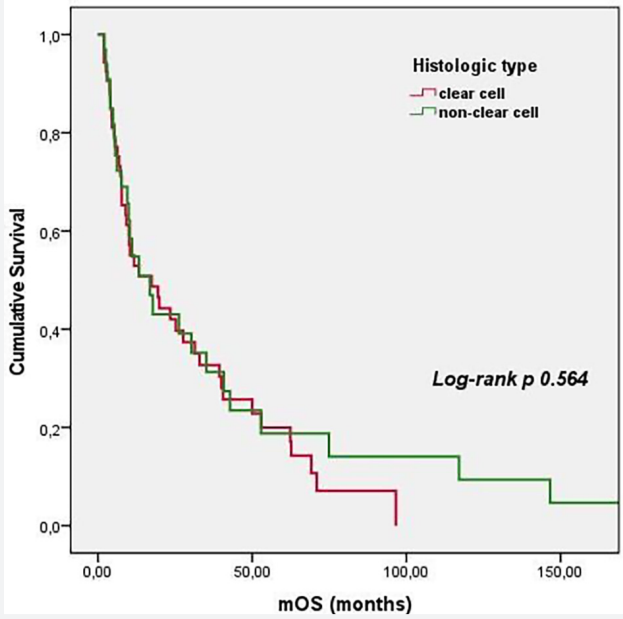

Figure 1. Kaplan-Meier curves for median overall survival (mOS) by histologic type

Table 2. Survival analysis of early stage patients

	mDFS (months) (95% CI)	p value	mOS (months) (95% CI)	p value
Overall	47.5 (22.6-72.3)		82.5 (55.4-109.5)	
Sex			**(Mean)**	
Female	66.8 (40.8-92.9)	0.069	191.8±31	**0.029**
Male	32.6 (22.3-42.9)		82.3±6	
Stage				
1	79.2 (55.6-102.7)	**0.001**	131.3 (116.2-146.4)	**0.002**
2	47.9 (22-73.9)		69 months (36.9-101.1)	
3	29.6 (6.6-52.5)		50.3 months (34.2-66.5)	
ECOG PS			**(Mean)**	
0	72.8 (56.9-88.8)	**0.001**	105±6.9	**0.020**
1	22.3 (15.5-29.1)		100.3±20	
2	13.3 (0-64.8)		78.7±16.3	
Histologic type				
Clear cell	47.5 (26-69)	0.327	68.3 (51.7-84.9)	0.147
Non-clear cell	59.1 (17.5-100.8)		135.7 (118-153.4)	

mDFS: Median disease-free survival, mOS: Median overall survival, CI: Confidence interval, ECOG PS: Eastern Cooperative Oncology Group Performance Status Scale

mOS was 50 months in patients with ECOG 0 and decreased to 1.2 months in patients with ECOG 3. Survival significantly shortened as the ECOG performance score worsened (p<0.001), as shown in Figure 4.

Survival analyses of advanced-stage patients are provided in Table 3.

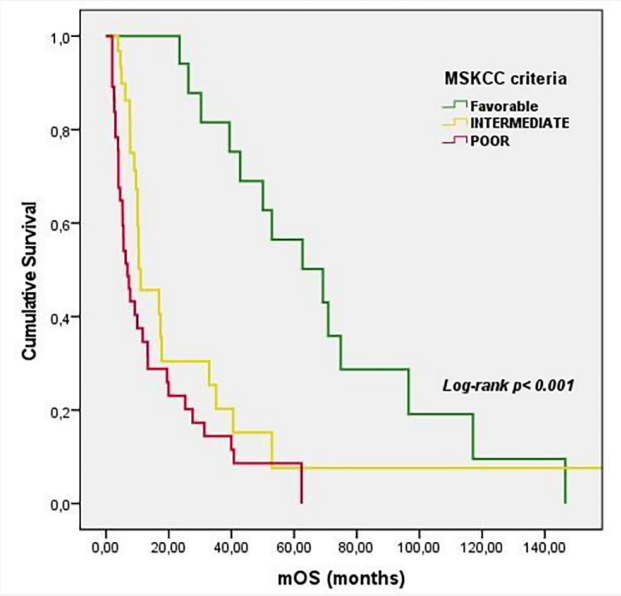

Figure 2. Kaplan-Meier curves for median overall survival (mOS) by MSKCC criteria

MSKCC: Memorial Sloan-Kettering Cancer Centre

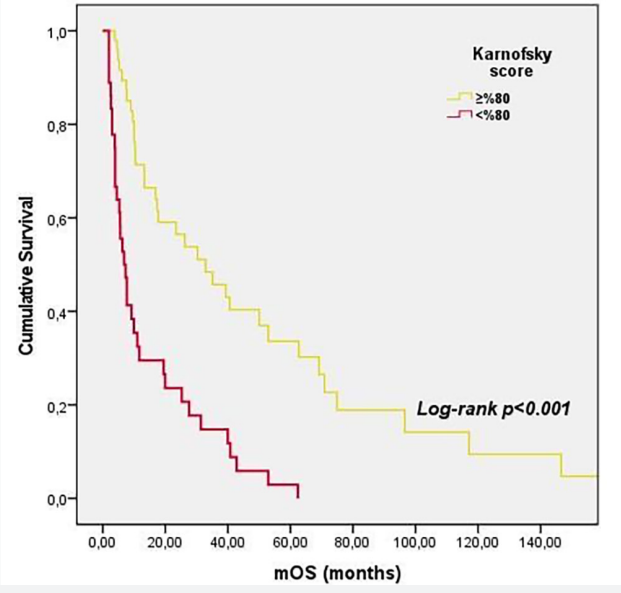

Figure 3. Kaplan-Meier curves for median overall survival (mOS) by Karnosfsky score

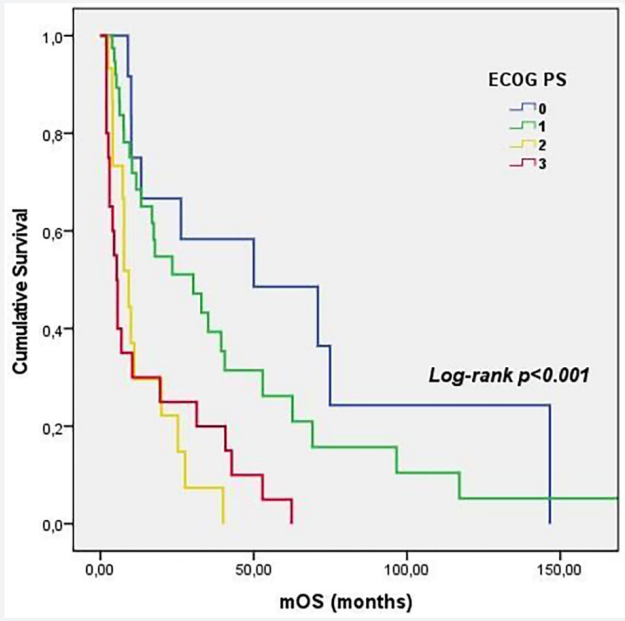

Figure 4. Kaplan-Meier curves for median overall survival (mOS) by ECOG PS

ECOG PS: Eastern Cooperative Oncology Group Performance Status Scale

Table 3. Survival analysis of stage 4 patients

	mOS (months) (95% CI)	p value
Overall	16.8 (8.4-25.3)	
Sex		
Female	9.9 (1-24.4)	**0.049**
Male	17.7 (1.8-33.6)	
Histologic type		
Clear cell	17.4 (5.1-29.6)	0.564
Non-clear cell	16.8 (8-25.6)	
Karnofsky score		
≥80%	32.9 (14.7-51)	**<0.001**
<80%	6.8 (4.4-9.2)	
MSKCC criteria		
Favorable	69.1 (39.3-99.1)	**<0.001**
Intermediate	11.1 (3.9-18.2)	
Poor	6.8 (4.3-9.4)	
ECOG PS		
0	50 (1-109)	
1	30.0 (11.8-48.8)	**<0.001**
2	9.2 (6.9-11.4)	
3	5.3 (2.8-7.7)	
Nephrectomy		
Yes	35.1 (6.7-63.5)	**0.001**
No	9.5 (4-15)	

mOS: Median overall survival, CI: Confidence interval, MSKCC: Memorial Sloan-Kettering Cancer Centre risk scores, ECOG PS: Eastern Cooperative Oncology Group Performance Status Scale

Results of Patients Treated with Sunitinib and Pazopanib

The general characteristics, median PFS (mPFS), and mOS durations of 114 patients who received TKI (sunitinib, pazopanib) were analyzed. Eighty patients received sunitinib and 34 patients received pazopanib. A CR was observed in 2 patients (2.8%), a PR in 24 patients (33.8%), SD in 15 patients (21.1%), and PD in 30 patients (42.3%). Among the patients receiving pazopanib, a PR was observed in 8 patients (27.6%), SD in 8 patients (27.6%), and PD in 10 patients (44.8%). Dose changes were made in 23 patients (30.3%) receiving sunitinib and in 3 patients (8.8%) receiving pazopanib due to adverse effects and the inability to tolerate the drug. The number of patients having adverse events at any grade was significantly higher in the sunitinib arm. The most common adverse events in the sunitinib arm were fatigue, hand-foot skin reaction, and gastrointestinal side effects. In the group receiving pazopanib, the most common adverse events were gastrointestinal adverse events, hematological adverse events, and high arterial blood pressure. Hypothyroidism occurred in 26 (32.5%) patients receiving sunitinib and 5 (14.7%) patients receiving pazopanib. The characteristics, treatment response, and adverse event status of TKI patients are shown in Table 4. In patients who received sunitinib, mPFS was 11.1 months and mOS was 18.1 months. In patients given pazopanib, mPFS was 12.2 months and mOS was 17.4 months. There was no statistically significant difference between the mPFS and mOS durations of patients receiving sunitinib and pazopanib (mPFS p=0.278, mOS p=0.403).

DISCUSSION

In our study, DFS, OS, and prognostic factors of 202 patients diagnosed with RCC were analyzed retrospectively. Additionally, the efficacy and adverse effects of both drugs were analyzed in patients treated with sunitinib and pazopanib in the first-line treatment for metastasis. The study included both early-stage (stage 1,2,3) and stage 4 patients, and analyses were performed separately for both groups. Of the 115 early-stage patients, 56 (49%) developed recurrence/metastasis during follow-up, with a mDFS of 47.5 months and a mOS of 82.5 months. As the stage progressed and ECOG performance score worsened, mDFS and mOS significantly decreased. Sex and histological subtypes were not associated with survival in early-stage patients. In the 86 patients with stage 4, mOS was 16.8 months, and in this group, the duration of mOS was significantly shorter in females, patients with poor Karnofsky and ECOG performance scores, patients with high MSKCC risk scores, and patients who could not undergo nephrectomy.

In our study, the objective response rates were similar in patients receiving sunitinib and pazopanib. In patients receiving sunitinib, the mPFS was 11.1 months and the mOS was 18.1 months, while in patients receiving pazopanib, the mPFS was 12.2 months and the mOS was 17.4 months. No statistically significant difference was observed between the two groups in survival. Many studies investigating the efficacy of pazopanib and sunitinib treatments have found that both drugs have similar efficacy in terms of PFS and OS durations in patients with metastatic RCC. Pazopanib shows non-inferiority compared to sunitinib[10-13]. Although their efficacy is similar, large-scale studies have reported that pazopanib is associated with less fatigue and a better general health-related quality of life than sunitinib[14,15]. Motzer et al.[13] reported that pazopanib treatment was associated with a lower incidence of some adverse effects such as fatigue and hand-foot skin reaction compared to sunitinib. In our study, while 30% of patients receiving sunitinib had a dose change, this rate was 8% in patients receiving pazopanib and was statistically significantly lower. When the adverse effect profiles were examined, gastrointestinal and hematological side effects and hypertension were similar for both agents. Fatigue, hand-foot skin reaction, and hypothyroidism were significantly more common in the sunitinib arm.

Table 4. Characteristics of patients given sunitinib and pazopanib, their treatment response and adverse events status

	Sunitinib n (%)	Pazopanib n (%)	p value
Sex			
Female	14 (17.5)	7 (20.6)	**0.69**
Male	66 (82.5)	27 (79.4)	
Stage at diagnosis			
1	12 (15)	4 (11.8)	
2	15 (18.8)	2 (5.9)	**0.13**
3	12 (15)	3 (8.8)	
4	41 (51.3)	25 (73.5)	
Histologic type			
Clear cell	49 (61.2)	25 (73.5)	0.14
Non-clear cell	31 (38.8)	9 (26.5)	
Response			
CR	2 (2.8)	0	
PR	24 (33.8)	8 (27.6)	0.689
SD	15 (21.1)	8 (27.6)	
PD	30 (42.5)	13 (44.8)	
Adverse events (any grade)			
Fatigue	32 (40)	2 (6)	
Hand-foot skin reaction	23 (28.7)	3 (9)	
Hypertension	11 (13.7)	4 (11.7)	**0.019**
Gastrointestinal	14 (17.5)	6 (17.6)	
Hematologic	11 (13.7)	4 (11.7)	
Endocrinologic	12 (15)	3 (9)	
Hypothyroidism	26 (32.5)	5 (14.7)	

CR: Complete response, PR: Partial response, SD: Stable disease, PD: Progressive disease

Although various scoring systems have been used to predict prognosis and decide on treatment in patients diagnosed with RCC, the MSKCC score is one of the most commonly used classifications to classify RCC patients into prognostic groups. After the MSKCC was defined, its effectiveness in predicting prognosis has been confirmed by various studies[16]. In addition, there are studies reporting that the MSKCC score is also prognostic in non-clear cell and sarcomatoid tumors[17,18]. In our study, the analysis models of patients who were metastatic at diagnosis and patients who developed metastasis during follow-up with the MSKCC score revealed prognostic features and survival times were statistically significantly shorter as the score worsened.

The effect of clear cell and non-clear cell histological subtypes on prognosis in RCC is controversial. de Velasco et al.[19] reported that the prognosis of patients with non-clear cell was worse in a study of more than four thousand patients, but the rate of sarcomatoid differentiation was 1.2% in the clear cell group and 26% in the non-clear cell group. Other studies show that the prognosis is better in the clear cell subtype[20,21]. Survival has been shown to be better in chromophobe subtype non-clear cell carcinomas[21]. In our study, mDFS was 47.5 months and mOS was 68.3 months in early-stage clear cell carcinoma, mDFS was 59.1 months and mOS was 135.7 months in the non-clear cell group; although OS was numerically longer in the non-clear cell group, it did not reach statistical significance. In our stage 4 patients, there was no OS difference between each clear cell and non-clear cell arms. We think that this difference in the literature may be due to heterogeneous patient groups in the non-clear cell group, especially tumors with sarcomatoid differentiation and tumors of collecting duct origin.

The KPS and the ECOG PS are established methods used to assess the functional status of cancer patients and are important in predicting patient outcomes. These scales are used to determine the eligibility of patients for clinical trials and to provide prognostic information. Karnofsky and ECOG PS scores have a strong correlation, and there is a high degree of agreement between the two scales, suggesting that they can be used interchangeably to a certain extent[22]. Intra-and inter-observer variability for both KPS and ECOG PS is very low, suggesting that assessments made by clinical oncologists using these scales are reliable in selecting patients for clinical trials[23]. In our study, we demonstrated the prognostic value of both performance scores in both early-stage and metastatic patients, and survival times were significantly shorter as the performance score worsened. We observed that both scores are correlated in showing performance status.

CONCLUSION

In our study, we investigated prognostic factors in patients diagnosed with RCC and performed survival analysis. We found that the disease stage and MSKCC risk score are prognostic. Additionally, we demonstrated the prognostic value of ECOG and KPS, which evaluate the performance status of patients. There was no survival difference between the histological subtypes. We also showed that sunitinib and pazopanib TKI treatments in metastatic first-line therapy were similar in terms of mPFS and mOS, but pazopanib was superior in terms of any grade of adverse events. This study shows that some inexpensive and easily accessible laboratory and clinical evaluations, as well as risk and performance scoring, are valuable and usable in determining prognosis in RCC patients.

Ethics

Ethics Committee Approval: Dicle University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (decision number: 25 date: 05.03.2020).

Informed Consent: Retrospective study.

Authorship Contributions

Concept: Ö.F.E., Design: Ö.F.E., Data Collection or Processing: Ö.F.E., Analysis or Interpretation: Ö.F.E., M.K., Literature Search: Ö.F.E., Writing: Ö.F.E.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Ferlay J, Ervik M, Lam F, Laversanne M, Colombet M, Mery L, et al. Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.who.int/today, accessed [12.05.2024].
2. Hanna KS. A review of checkpoint inhibitors in the management of renal cell carcinoma. Journal of Oncology Pharmacy Practice. 2020;26:445-58.
3. Lam JS, Shvarts O, Leppert JT, Pantuck AJ, Figlin RA, Belldegrun AS. Postoperative surveillance protocol for patients with localized and locally advanced renal cell carcinoma based on a validated prognostic nomogram and risk group stratification system. J Urol. 2005;174:466-72.
4. de Peralta-Venturina M, Moch H, Amin M, Tamboli P, Hailemariam S, Mihatsch M, et al. Sarcomatoid differentiation in renal cell carcinoma: a study of 101 cases Am J Surg Pathol. 2001;25:275-84.
5. Pichler R, Compérat E, Klatte T, Pichler M, Loidl W, Lusuardi L, et al. Renal Cell Carcinoma with Sarcomatoid Features: Finally, New Therapeutic Hope? Cancers (Basel). 2019;11:422.
6. Motzer RJ, Hutson TE, Tomczak P, Michaelson MD, Bukowski RM, Rixe O, et al. Sunitinib versus interferon alfa in metastatic renal-cell carcinoma. N Engl J Med. 2007;356:115-24.
7. Wu J, Ren Y, Xie J, Li, D. Targeting CTLA-4 in Cancer: Biological Insights with a Focus on Renal Cell Carcinoma. Annals of Urologic Oncology. 2022;5:68-74.
8. Díaz-Montero CM, Rini BI, Finke JH. The immunology of renal cell carcinoma. Nat Rev Nephrol. 2020;16:721-35.
9. Kase AM, George DJ, Ramalingam S. Clear Cell Renal Cell Carcinoma: From Biology to Treatment. Cancers (Basel). 2023;15:665.

10. Frampton JE. Pazopanib: a Review in Advanced Renal Cell Carcinoma. Target Oncol. 2017;12:543-54.

11. Ruiz-Morales JM, Swierkowski M, Wells JC, Fraccon AP, Pasini F, Donskov F, et al. First-line sunitinib versus pazopanib in metastatic renal cell carcinoma: Results from the International Metastatic Renal Cell Carcinoma Database Consortium. European journal of cancer. 2016;65:102-8.

12. Beaumont, J., Salsman, J., Diaz, J., Deen, K., McCann, L., Powles, T., et al. Quality-adjusted time without symptoms or toxicity analysis of pazopanib versus sunitinib in patients with renal cell carcinoma. Cancer. 122:1108-15.

13. Motzer RJ, Hutson TE, Cella D, Reeves J, Hawkins R, Guo J, et al. Pazopanib versus sunitinib in metastatic renal-cell carcinoma. The New England journal of medicine. 369;8:722-31.

14. Escudier B, Porta C, Bono P, Powles T, Eisen T, Sternberg CN, et al. Randomised, controlled, double-blind, cross-over trial assessing treatment preference for pazopanib versus sunitinib in patients with metastatic renal cell carcinoma: PISCES Study. Journal of clinical oncology: official journal of the American Society of Clinical Oncology. 2014;32:1417-8.

15. Frampton, JE. Pazopanib: A Review in Advanced Renal Cell Carcinoma. Targeted Oncology. 2017;12:543-54.

16. Fiala O, Finek J, Poprach A, Melichar B, Kopecký J, Zemanova M, et al. Outcomes According to MSKCC Risk Score with Focus on the Intermediate-Risk Group in Metastatic Renal Cell Carcinoma Patients Treated with First-Line Sunitinib: A Retrospective Analysis of 2390 Patients. Cancers. 2020;12:808.

17. Kim JK, Kim SH, Song MK, Joo J, Seo SI, Kwak C, et al. Application of the International Metastatic Renal Cell Carcinoma Database Consortium and Memorial Sloan Kettering Cancer Center Risk Models in Patients with Metastatic Non-Clear Cell Renal Cell Carcinoma: A Multi-Institutional Retrospective Study Using the Korean Metastatic Renal Cell Carcinoma Registry. Cancer Res Treat. 2019;51:758-68.

18. Korenbaum C, Pierard L, Thiéry A, Story F, Lindner V, Lang H, et al. Treatments, Outcomes, and Validity of Prognostic Scores in Patients with Sarcomatoid Renal Cell Carcinoma: A 20-Year Single-Institution Experience. Clinical Genitourinary Cancer. 2018;16:e577-86.

19. de Velasco G, McKay RR, Lin X, Moreira RB, Simantov R, Choueiri TK. Comprehensive Analysis of Survival Outcomes in Non-Clear Cell Renal Cell Carcinoma Patients Treated in Clinical Trials. Clin Genitourin Cancer. 2017;15:652-60.

20. Vera-Badillo FE, Templeton AJ, Duran I, Ocana A, de Gouveia P, Aneja P, et al. Systemic therapy for non-clear cell renal cell carcinomas: a systematic review and meta-analysis. European urology. 2015;67:740-9.

21. Motzer RJ, Bacik J, Mariani T, Russo P, Mazumdar M, Reuter V. Treatment outcome and survival associated with metastatic renal cell carcinoma of non-clear-cell histology. J Clin Oncol. 2002;20:2376-81.

22. Buccheri G, Ferrigno D, Tamburini M. Karnofsky and ECOG performance status scoring in lung cancer: a prospective, longitudinal study of 536 patients from a single institution. Eur J Cancer. 1996;32A:1135-41.

23. Roila F, Lupattelli M, Sassi M, Basurto C, Bracarda S, Picciafuoco M, et al. Intra and interobserver variability in cancer patients' performance status assessed according to Karnofsky and ECOG scales. Ann Oncol. 1991;2:437-9.