Original Article

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Can We Predict Recurrence of pT1-2 Renal Cell Carcinoma?

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Abstract

Objective: Some prognostic models have been described for localized and metastatic renal cell carcinoma (RCC). The European Association of Urology guidelines on RCC recommend using these models. However, there is no model for T1 and T2. The study evaluated the risk factors for recurrence in T1 and T2 RCC.
Materials and Methods: Data of 4823 renal tumor patients from the Renal Tumor Database of the Association of Urooncology in Turkey were evaluated. Of 4823 patients, 1845 RCC patients with pathological T1 or T2 were included in this study. The patients were divided into two groups according to the recurrence status. Anatomical, histological, and clinical prognostic factors were statistically compared between the groups. Afterwards, multivariate analysis was performed for the variables that were found to be statistically significant.
Results: The mean follow-up time was 30 (4-180) months. Of 1845 RCC patients, 117 (6.3%) had recurrence. Univariate analysis revealed statistically significant differences between age, preoperative hemoglobin, albumin, neutrophil, alkaline phosphates, platelet and calcium values, histological subtype, Fuhrman grade, surgical technique (radical or partial), and pathological stage in the groups. However, in multivariate analysis, only pathological stage was found to be a risk factor for recurrence (2.17 95%, 1.25-3.77).
Conclusions: The results of our study show that it is difficult to design a prognostic model for the recurrence of pT1 and pT2 RCC. We suggest that patients with a higher tumor diameter should be followed up more frequently.
Keywords: RCC, pT1-2, recurrence, prediction of recurrence

Introduction

Renal cell carcinoma (RCC) is the most frequently occurring renal malignant tumor, accounting for 2-3% of all adult malignant tumors (1). The once classical triad of abdominal mass, pain, and macroscopic hematuria is now recognized to be rare. RCC is incidentally diagnosed at an early stage with the widespread use of ultrasonography and computed tomography in the last two decades. Partial or radical nephrectomy is the standard treatment for cT1-2 RCC. After standard treatment of RCC, the 5-year recurrence rates of T1 and T2 RCC are 9% and 32%, respectively (2). Some prognostic models have been described for predicting recurrence and/or progression in localized and metastatic RCC. The European Association of Urology (EAU) guidelines on RCC recommend using these models (3). However, there is no model for T1 and T2 RCC. The study evaluated risk factors for recurrence in T1 and T2 RCC in Turkey using the Renal Tumor Database of the Turkish Urooncology Association.

Materials and Methods

Data of 4823 patients who underwent partial or radical nephrectomy for RCC from 2000 to 2019 were retrospectively investigated. These data were obtained from the Renal Tumor

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Database of the Turkish Urooncology Association in Turkey. Of 4823 patients, 1845 RCC patients with pathological T1 or T2 stage were included in this study. The pathological stages of the patients were identified according to the TNM 2017 Classification. Exclusion criteria were incomplete data, patients with pathological T3-4 stage and/or metastasis (lymph node and/or distant visceral metastasis), patients aged 18 years, and patients who underwent other procedures without surgical resection, such as microwave or radiofrequency ablation. The Manisa Celal Bayar University Faculty of Medicine Ethics Committee approved the study protocol (decision no: 20.478.486/2044, date: 11.10.2023).

Statistical Analysis

The patients were divided into two groups according to the recurrence status. Anatomical, histological, and clinical prognostic factors were statistically compared between the two groups. Afterwards, multivariate analysis was performed for the variables that were found to be statistically significant. Statistical analysis was performed using the SPSS software package version 22.0 (Statistical Package for Social ScienceTM, Chicago, IL, USA) and $p<0.05$ was considered to be statistically significant.

Results

The mean age of patients (n=1845) was 57.07±12.32. The mean follow-up time was 30 (4-180) months. Of 1845 RCC patients, 117 (6.3%) had recurrence. Univariate analysis revealed statistically significant differences between age, preoperative hemoglobin, albumin, neutrophil, alkaline phosphates, platelet and calcium values, histological subtype, Furhman grade, surgical technique (radical or partial), and pathological stage in the groups. The results of the univariate analysis are presented in Tables 1 and 2. Then, the variables that were found to be statistically significant differences between the two groups were subjected to multivariate analyses. However, in multivariate analysis, only pathological stage was found to be a risk factor for recurrence (2.17 95%, 1.25-3.77).

Discussion

Generally, during the last two decades until recently, there has been an annual increase of approximately 2% in the incidence of RCC both worldwide and in Europe. The higher incidence is hypothesized to be due to a higher prevalence of small renal masses in settings where abdominal imaging is more ubiquitous. In 1993-2004, 54.7%, 10.6%, 16.1%, and 18.6% of clear cell RCC (ccRCC) tumors in the National Cancer Database were classified as stage I, II, III, and IV, respectively (4). In a 2004-2015 Surveillance, Epidemiology, and End Results (SEER) database cohort (77% had ccRCC), the pathologic tumor, node, metastasis (TNM) stage was I (64.3%), II (10.9%), III (16.8%), and IV (8%) (5). Therefore, it is more important to follow-up on local RCC because its incidence has been increasing. The results of this study show that the only prognostic factor in recurrence of local stage RCC (T1 and T2) is the pathological stage of the tumor. This indicates a relationship between tumor size and risk of recurrence. Similar to the results of our study, in a 2004-2015

Table 1. Comparison of demographic data and preoperative laboratory results between the recurrent and non-recurrent groups

		Recurrent group	**Non-recurrent group**	**p-value**
Age (years)	Mean ± SD (n)	61.19±10.62 (145)	56.90±12.40 (1850)	<0.001**
BMI (kg/m^2)	Mean ± SD (n)	28.70±5.33 (28)	28.05±4.86 (534)	0.531
Hospitalization time (days)	Median (n)	5 (77)	4 (1413)	<0.05*
Time (days) from diagnosis to surgery	Median (n)	31 (102)	36 (1628)	0.061
Smoking (pack/year)	Median (n)	5.5 (254)	5 (1850)	0.663
Preoperative laboratory		**Recurrent group**	**Non-recurrent group**	**p-value**
Hemoglobin (g/dL)	Mean ± SD (n)	12.78±2.14 (133)	13.74±1.76 (1755)	<0.001**
White blood count (/µL)	Mean ± SD (n)	8560±2630 (80)	8253±2831 (1452)	0.165
Lymphocyte (/µL)	Mean ± SD (n)	1465±1640 (50)	1177±1265 (1075)	0.205
Neutrophil	Mean ± SD (n)	6191±2599 (51)	5556±1830 (1089)	0.122
Platelet* 1000	Mean ± SD (n)	278.545±94.421 (80)	256.915±77.334 (1446)	<0.05*
Erythrocyte sedimentation rate	Mean ± SD (n)	38.45±38.69 (11)	26.84± 2.87 (111)	0.366
C-reactive protein (mg/L)	Mean ± SD (n)	58.07±89.67 (15)	118.83±239.25 (172)	0.829
Creatinine (mg/dL)	Mean ± SD (n)	0.99±0.36 (136)	0.97±0.68 (1740)	0.100
Aspartate aminotransferase (U/L)	Mean ± SD (n)	21.82±10.69 (66)	22.07±10.55 (1171)	0.070
Alanine transaminase (U/L)	Mean ± SD (n)	22.04±14.95 (65)	23.54±15.39 (1165)	0.344
Alkaline phosphatase (U/L)	Mean ± SD (n)	110.38±77.83 (44)	81.49±32.82 (748)	<0.05*
Lactate dehydrogenase (U/L)	Mean ± SD (n)	196.38±59.74 (47)	213.82±101.49 (587)	0.344
Albumin (g/dL)	Mean ± SD (n)	4.08±0.57 (60)	4.26±0.50 (942)	<0.05*
Calcium (mg/dL)	Mean ± SD (n)	9.30±0.75 (60)	9.44±0.71 (898)	<0.05*

SD: Standard deviation, BMI: Body mass index
*p<0.05 was considered statistically significant,
**p<0.001 was considered statistically significant

SEER database cohort noticed that 5 years survival of T1 and T2 RCC were 97.4% and 89.9%, respectively (5). All of the findings show that tumor size is important for the follow-up of local stage RCC. If the tumor size is larger, we should be more careful in the follow-up of RCC.

Histological subtypes of RCC are another important prognostic factor, and on univariate analysis of some studies, patients with chromophobe RCC vs. papillary RCC vs. ccRCC had a better prognosis (6,7). Univariate analysis of our study showed that the recurrence rate of ccRCC is significantly higher than that of chromophobe and papillary RCC (Table 2). The results of multivariate analyses in our study and previous studies indicated that the histological subtype of RCC is not a prognostic factor for predicting recurrence. EAU Guidelines on RCC noticed that prognostic information provided by the RCC type is lost when stratified according to tumor stage (3).

Sarcomatoid features in RCC have been evaluated as another prognostic factor for predicting recurrence. The findings of our study showed that the recurrence rate of RCC with sarcomatoid differentiations (32.0%) is higher than that of RCC without sarcomatoid features (7.1%) on univariate analysis (Table 2). Trudeau et al. (8) compared 5-year cancer-specific mortality estimates of sarcomatoid RCC (sRCC) and ccRCC. They found that 5-year cancer-specific mortality estimates of sRCC and ccRCC in patients with stage 1-2 RCC were 32% and 6%, respectively. When we analyzed the recurrence rates according to Fuhrman grade, the recurrence rates in RCC patients with Fuhrman grades I, II, III and IV were 1.9%, 6.0%, 14.8% and 32.1%, respectively. This was a statistically significant finding on univariate analysis ($p<0.001$). However, Fuhrman grade, like sarcomatoid features, was not a statistically significant factor in multivariate analysis to predict recurrence in our study.

Preoperative hematological and biochemical parameters in RCC have been investigated as prognostic factors to predict recurrence and create a nomogram or prognostic model. Although some of these parameters are used in prognostic models of Memorial

Table 2. Comparison of gender, preoperative platelet count, surgical technique, postoperative creatinine rise, and pathological features between recurrent and non-recurrent groups

		Recurrent group n (%)	Non-recurrent group n (%)	p-value
Gender	Female	38 (5.4)	667 (94.6)	<0.05*
	Male	107 (8.3)	1183 (91.7)	
Preoperative platelet count *1000	<400	72 (4.9)	1384 (95.1)	<0.05*
	>400	8 (11.4)	62 (88.6)	
Nephrectomy	Partial	23 (2.5)	897 (97.5)	<0.001**
	Radical	120 (11.3)	942 (88.7)	
Postoperative creatinine levels rising	Yes	28 (9.7)	261 (90.3)	<0.05*
	No	43 (4.7)	879 (95.3)	
Pathological features		**Recurrent group n (%)**	**Non-recurrent group n (%)**	**p-value**
T stage	T1a	50 (4.6)	1029 (95.4)	<0.001**
	T1b	54 (8.6)	577 (91.4)	
	T2a	28 (13.8)	175 (86.2)	
	T2b	13 (15.9)	69 (84.1)	
Fuhrman grade	Grade 1	4 (1.9)	209 (98.1)	<0.001**
	Grade 2	55 (6.0)	865 (94.0)	
	Grade 3	53 (14.8)	305 (82.5)	
	Grade 4	17 (32.1)	36 (67.9)	
Surgical margin	Negative	136 (7.3)	1734 (92.7)	0.276
	Positive	3 (3.6)	81 (96.4)	
Pathological necrosis	Yes	17 (9.0)	172 (91.0)	0.450
	No	99 (6.8)	1360 (93.2)	
Sarcomatoid differentiation	Yes	8 (32.0)	17 (68.0)	<0.05*
	No	121 (7.1)	1584 (92.9)	
Microvascular invasion	Yes	7 (16.3)	36 (83.7)	<0.05*
	No	106 (8.0)	1211 (92.0)	
Histological subtypes	Clear cell	125 (8.6)	1323 (91.4)	<0.001**
	Chromophobe	1 (0.4)	223 (99.6)	
	Papillary types 1 and 2	19 (5.9)	304 (94.1)	

*p<0.05 was considered statistically significant,
**p<0.001 was considered statistically significant

Sloan Kettering Cancer Center and International Metastatic Renal-cell Carcinoma Database Consortium Score for metastatic RCC, none of them are used in prognostic models created for localized RCC (3). In our study, some of them were found to be statistically significant prognostic factors for recurrence on univariate analysis in stage 1-2 RCC patients. However, on multivariate analysis, none of them was a statistically significant factor to predict recurrence.

Study Limitations

The limitation of our study is that the rate of recurrence was small because the patients had local stage RCC. Therefore, it was difficult to perform multivariate and subgroup analyses.

Conclusion

The results of our study show that there are some prognostic factors to predict recurrence in patients with T1-2 RCC on univariate analysis. However, on multivariate analysis, only tumor stage was found to be a statistically significant prognostic factor. Therefore, it is difficult to create a prognostic model for T1-2 RCC recurrence. On the other hand, we found that tumor stage in T1-2 RCC is a prognostic factor for recurrence. In summary, the risk of recurrence may increase as the tumor size increases in patients with T1-2 RCC. We suggest that patients with larger RCC should be followed up more carefully.

Ethics

Ethics Committee Approval: The Manisa Celal Bayar University Faculty of Medicine Ethics Committee approved the study protocol (decision no: 20.478.486/2044, date: 11.10.2023).

Informed Consent: Retrospective study.

Authorship Contributions

Concept: O.Ü., T.M., Design: O.Ü., Data Collection or Processing: S.B., V.İ., E.Ö., B.A., S.Y., E.C.B., N.A., S.S., Analysis or Interpretation: G.A., Literature Search: E.S., Writing: O.Ü.

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