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The Effect of Framingham Score on the Oncological Outcomes in Localized (T1-T2 Stage) Renal Cell Carcinoma Patients

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Abstract

Objective: To evaluate the effect of cardiovascular disease risk on local recurrence, distant metastasis development and cancer-specific survival in patients with localized (stage 1 and 2) renal cell carcinoma (RCC).

Materials and Methods: Data of patients who underwent partial or radical nephrectomy due to pathological stage 1 and 2 RCC between September 2009 and July 2016 were retrospectively evaluated. Ninety-six patients with fully accessible data were included in the study. Demographic data, histological tumor type, Fuhrman grading, local recurrence, metastasis and survival after nephrectomy were recorded. Framingham risk score, which predicts cardiovascular disease within 10 years, was calculated in all patients. The patients were divided into three groups as low (group 1), moderate (group 2) and high risk (group 3).

Results: Mean age of patients was 58.66±10.55 years at the time of nephrectomy. Nine (9.4%) patients had local recurrence, 12 (12.5%) had distant metastasis and 11 (11.5%) died due to cancer during a median follow-up period of 57 (6-102) months. Regarding intergroup comparison, local recurrence rate (21.9%, p=0.012) and distant metastasis rate (25%, p=0.025) were significantly higher in group 3, and predicted recurrence-free survival (66.4 months, p=0.005), metastasis-free survival (77 months, p=0.017) and cancer-specific survival (79.9 months, p=0.024) were found to be significantly lower. In univariate analysis, body mass index, total cholesterol level, estimated glomerular filtration rate and Framingham risk score were independent predictive factors for local recurrence, distant metastasis development and cancer-specific survival. In multivariate analysis, body mass index, estimated glomerular filtration rate and Framingham risk score were more significant.

Conclusion: Patients who are at high risk of developing cardiovascular disease have more local recurrence, distant metastasis and cancer-specific mortality rates, even though nephrectomy is performed due to localized RCC. Therefore, we suggest that these patients should be followed more carefully in the post-nephrectomy period.

Keywords: Cardiovascular disease risk, Framingham risk score, nephrectomy, oncologic outcomes, renal cell carcinoma

Introduction

Renal cell carcinoma (RCC) with increased rates of incidental detection during the localized stage (stage 1-2) with a small size accounts for 2-3% of all cancers (1). Its incidence increases in the sixth and seventh decades, and known predisposing factors are smoking, obesity and hypertension (2).

Although the presence of tumor-related anatomical and histological factors [tumor-node-metastasis (TNM) stage, Fuhrman tumor grade, histological type, tumor size, presence of necrosis, etc.] and patient-related factors (clinical signs, symptoms, general health status, laboratory findings, molecular factors) is known (3), the importance of new molecular markers continues to be investigated with current studies (4,5,6). In localized RCC patients, local recurrence or distant metastasis rates after partial or radical nephrectomy have been reported to be 20-40% (7). The effects of presence and components of metabolic syndrome on oncologic outcomes in localized RCC have been investigated in many studies. The common belief in these studies is that the metabolic syndrome is a poor prognostic factor for RCC, that it increases the incidence of RCC approximately 4-6 times, leads to an increase in tumor size and stage, and significantly reduces progression-free survival (PFS) (8,9,10). Hypertension was found to be the worst prognostic risk factor in the publications investigating the effects of

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individual metabolic syndrome components on oncologic outcomes in RCC (11,12). However, there are no studies in the literature that predict post-nephrectomy outcomes according to developing 10-year cardiovascular disease risk.

In our study, we aimed to investigate the effect of cardiovascular disease risk, calculated according to Framingham score before nephrectomy, on the local recurrence, distant metastasis and cancer-related mortality rates in patients with pathologic stage 1-2 RCC.

Materials and Methods

We retrospectively evaluated 148 patients who underwent partial or radical nephrectomy due to localized RCC, and whose pathological diagnosis was stage 1 or 2 RCC according to TNM classification in our clinic between September 2009 and July 2016. The demographic data of the patients, histological tumor type, Fuhrman grading, presence of necrosis, tumor side, localization, size, type of surgery, follow-up period after nephrectomy, local recurrence, metastasis and survival rates were recorded. Estimated glomerular filtration rate (eGFR), calculated by the short-term Modification of Diet in Renal Disease (MDRD) formula using preoperative creatinine, age, gender and race, was recorded.

Framingham Risk Score

The Framingham risk score was prepared according to long-term studies of National Cholesterol Education Program Adult Treatment Panel 3 (NCEP ATP 3) and National Heart, Lung and Blood Institute and it is based on research in 1976. It was first tried in 1998 in daily practice and it is used to estimate the 10-year cardiovascular (myocardial infarction, coronary death, angina, etc.) risk of an individual. Reliability and validity have been provided by various studies (13). The Framingham score, which is one of the most commonly used risk calculations, systematically predicts the risk of cardiovascular disease and related mortality by systematic mathematical equations (14). The aim of this risk score is to determine measurable and preventable risk factors that can affect the development of cardiovascular disease, to provide lifestyle and behavior change in patients at risk and to determine appropriate treatment.

The Framingham risk calculator, developed for patients between the ages of 30-74, only calculates 10-year cardiovascular event risk (total of non-fatal and fatal coronary events). The parameters used in the Framingham risk score include risk factors associated with coronary heart disease, such as age, gender, blood pressure, total cholesterol, high density lipoprotein (HDL) levels, smoking, and diabetes. Scoring is performed for each parameter and the total score is calculated. The percentages that correspond to the specified score range refer to the 10-year risk of developing cardiovascular disease separately for men and women. According to this, <10% indicates a low-risk, 10-20 % a moderate-risk and >20% a high risk (15). This risk score is both easy to implement and does not require additional invasive intervention or cost because the necessary data can be easily obtained in clinical practice.

The data required to calculate Framingham risk score of patients included in the study, which include age, gender, total cholesterol, HDL level, systolic blood pressure, use of antihypertensive treatment, smoking, and diabetes, were obtained from hospital archive and patient information system. These data were used in the calculation of Framingham score in the week immediately preceding nephrectomy. Ninety-six patients with complete data were included in the study without randomization. According to the Framingham risk score, the patients were divided into three groups as low-risk (<10%), moderate-risk (10-20%) and high risk (> 20%) respectively, and were named as group 1, 2 and 3, respectively. Three groups were compared in terms of oncologic outcomes.

Statistical Analysis

To compare the differences between the three groups, Pearson chi-square was used for categorical variables, One-way analysis of variance (ANOVA) or Kruskal-Wallis test were used for continuous variables. Tukey or Dunn-Bonferroni tests were applied for multiple comparisons. Kaplan-Meier was used for survival analysis and Cox regression analysis was used to determine the variables that affect this. Spearman test was used for correlation analysis. Analysis was performed using IBM SPSS Statistics 21 (IBM, Armonk, NY USA) software. $p<0.05$ was considered statistically significant.

Results

The mean age of the 96 patients included in the study was 58.66±10.55 years, and 56 (58.3%) were male and 40 (41.7%) were female. During the median follow-up period of 57 (6-102) months, nine (9.4%) patients had local recurrence, 12 (12.5%) had distant metastasis and 11 (11.5%) died due to cancer. Distant metastases were seen in lung in six patients, bone in two patients and liver in four patients. Demographic, pathological, clinical data and oncologic outcomes of the patients are shown in Table 1.

Regarding intergroup comparisons, local recurrence rate (21.9%, p=0.012) and distant metastasis rate (25%, p=0.025) were significantly higher in group 3 (Table 1). The predicted recurrence-free survival in group 3 (66.4 months) was significantly lower than in group 1 (98.9 months) and group 2 (99.2 months) (p=0.021 and p=0.010, respectively). No significant difference was observed between the predicted recurrence-free survivals of the patients in group 1 and group 2 (p=0.935) (Table 2, Figure 1).

The predicted metastasis-free survival in group 3 (77 months) was significantly lower than in group 1 (92.2 months) (p=0.013). There was no significant difference between survival in group 2 (94.5 months) and group 1 and group 3 patients (p=0.404 and p=0.061, respectively) (Table 2, Figure 2).

The predicted cancer-specific survival in group 3 (79.9 months) was significantly lower than in group 1 (102 months) (p=0.007). There was no significant difference between predicted cancer-specific survival in group 2 (94.7 months) and group 1 and group 3 (p=0.401 and p=0.128, respectively) (Table 2, Figure 3).

In the univariate analysis, body mass index (BMI), total cholesterol level, eGFR and Framingham risk score were independent predictive factors for local recurrence, distant metastasis and cancer-specific survival. In multivariate analysis,

Table 1. Demographic, pathological, clinical data and oncologic outcomes of patients					
Parameters	**Group 1 (n=31)**	**Group 2 (n=33)**	**Group 3 (n=32)**	**Total (n=96)**	**p**
Age, mean ± standard deviation	54.84±11.17[a]	61.30±9.32[b]	59.63±10.39[ab]	58.66±10.55	† 0.039*
Gender (n,%) Male Female	 17 (54.8) 14 (45.2)	 19 (57.6) 14 (42.4)	 20 (62.5) 12 (37.5)	 56 (58.3) 40 (41.7)	‡ 0.822
BMI (kg/m^2) (median, 25th -75th percentile)	23.3 (21.3-24.4)[a]	23.6 (21.9-26.2)[a]	27.6 (24.5-29.0)[b]	24.2 (22.3-26.8)	§ 0.226/<0.001/<0.001*
Smoking Yes No	 13 (41.9) 18 (58.1)	 22 (66.7) 9 (27.3)	 25 (78.1) 9 (21.9)	 60 (62.5) 36 (37.5)	‡ 0.016*
Hypertension Yes No	 1 (3.2) 30 (96.8)	 9 (27.2) 24 (72.8)	 17 (53.1) 15 (46.9)	 27 (28.1) 69 (71.9)	‡ <0.001*
Diabetes Yes No	 3 (9.7) 28 (90.3)	 5 (15.2) 28 (84.8)	 15 (46.9) 17 (53.1)	 23 (23.9) 73 (76.1)	‡ 0.001*
Surgery Radical Partial	 20 (64.5) 11 (35.5)	 23 (69.7) 10 (30.3)	 25 (78.1) 7 (21.9)	 68 (70.8) 28 (29.2)	‡ 0.486
Tumor side Right Left	 14 (45.2) 17 (54.8)	 17 (51.5) 16 (48.5)	 15 (46.9) 17 (53.1)	 46 (47.9) 50 (52.1)	‡ 0.87
Tumor localization Upper pole Middle pole Lower pole Hilum	 9 (29) 8 (25.8) 12 (38.7) 2 (6.5)	 7 (21.2) 8 (24.2) 14 (42.5) 4 (12.1)	 10 (31.3) 6 (18.8) 7 (21.9) 9 (28)	 26 (27) 22 (22.9) 33 (34.3) 15 (15.8)	‡ 0.209
Pathological tumor size (cm) (median, 25th -75th percentile)	4.4 (3.2-5.5)	4.6 (2.7-6)	4.5 (3-5.8)	4.4 (3.02-5.95)	§ 0.98
Histological subtype, (n,%) Clear cell Papillary Chromophobe Other	 22 (71) 4 (12.9) 3 (9.7) 2 (6.4)	 25 (75.8) 4 (12.1) 2 (6.1) 2 (6.1)	 23 (71.9) 6 (18.8) 1 (3.1) 2 (6.2)	 70 (72.9) 14 (14.5) 6 (6.3) 6 (6.3)	‡ 0.899
Fuhrman grade (n,%) 1-2 3-4	 18 (58) 13 (42)	 22 (66.7) 11 (33.3)	 22 (68.8) 10 (31.2)	 62 (64.5) 34 (35.5)	‡ 0.644
Pathological stage (n,%) T1a T1b T2a-T2b	 13 (41.9) 16 (51.6) 2 (6.4)	 15 (45.5) 13 (39.4) 5 (15.2)	 17 (53.1) 11 (34.4) 4 (12.5)	 45 (46.8) 40 (41.7) 11 (11.5)	‡ 0.604
TNM stage (n,%) Stage 1 Stage 2	 29 (93.5) 2 (6.5)	 28 (84.8) 5 (15.2)	 28 (87.5) 4 (12.5)	 85 (88.5) 11 (11.5)	‡ 0.537
Presence of necrosis (n,%) Yes No	 4 (12.9) 27 (87.1)	 9 (27.3) 24 (72.7)	 7 (21.9) 25 (78.1)	 20 (20.8) 76 (79.2)	‡ 0.362
eGFR (median, 25th -75th percentile)	95.46 (78.98-108.56)[a]	81.96 (69.27-91.38)[b]	78.97 (72.44-89.01)[b]	83.25 (73.23-97.88)	§ 0.007/0.003/0.637*
Follow-up period, median (min-max) month	59 (13-102)	57 (14-102)	50 (6-100)	57 (6-102)	§ 0.571
Local recurrence rate (n,%)	1 (3.2)	1 (3.0)	7 (21.9)	9 (9.4)	‡ 0.012*
Distant metastasis rate (n,%)	1 (3.2)	3 (9.1)	8 (25)	12 (12.5)	‡ 0.025*
Cancer-specific survival rate (%)	96.8	90.9	78.1	88.5	‡ 0.059

a, b, c: Groups with statistically significant differences were shown with different letters
There is no statistical difference between the groups indicated by the same letter.
ab: Group with no statistically significant difference from other two groups
† ANOVA ‡ Chi-square § Kruskal-Wallis * p <0.05 (There is a significant difference between groups)
BMI: Body mass index, TNM: Tumour-node-metastasis,
eGFR: Estimated glomerular filtration rate

BMI, eGFR and Framingham risk score were found to be more significant (Table 3). In addition, according to Spearman correlation analysis, a significant negative correlation was found between eGFR and Framingham risk score (r=-0.380, p <0.001) (Figure 4).

Discussion

The tumor-related anatomical and histological factors affecting prognosis in RCC are TNM stage, Fuhrman tumor grade, RCC histological subtype, and tumor size. Nowadays, many nomograms and models have been defined for the development of recurrence and progression in both localized and metastatic disease before and after nephrectomy. The most important of these models as independent prognostic factors are TNM stage, Fuhrman degree and patient performance status.

The pathologic tumor stage in RCC is the most important prognostic factor alone, and the 5-year survival rate in T1-2N0M0 is 70-90% (16). The 10-year cancer-specific survival rates for pathological stage T1a, T1b, T2 are 90-95%, 80-85% and 75%, respectively (17). Large-sized, organ-confined tumors have been found to have a greater degree of clear cell tumor histology and a higher grade of Fuhrman (18).

In a multicentre study involving 5332 patients, the 5-year cancer-specific survival rates reported by Novara et al. (19) were 94.9%, 92.6%, 85.4% and 70% for pT1a, pT1b, pT2a, pT2b, respectively. In a current study involving T1, T2 and T3a patients, local or distant recurrence was 21.57% and cancer-specific survival was 78.43% at 50.8±18.1 months follow-up (20).

In RCC, the Fuhrman nuclear grade revealed a link between tumor stage, size, nodal involvement and systemic metastasis (21). When all pathological stages were compared, 5-year

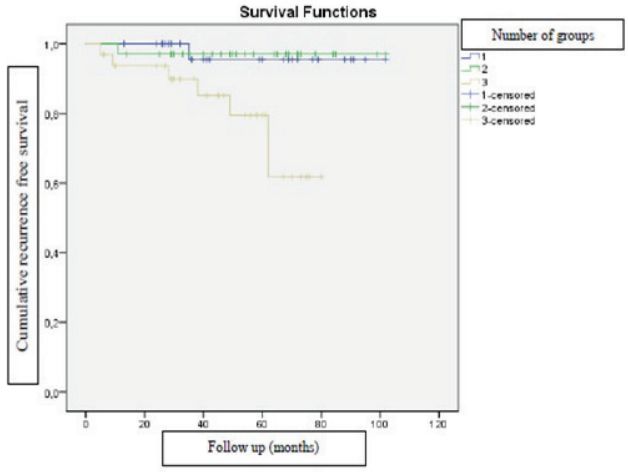

Figure 1. Graph of Kaplan-Meier analysis for predicted recurrence-free survival in three groups

Table 2. Predicted recurrence-free, metastasis-free and cancer-specific survival for three groups

	Mean	% 95 CI		Median	% 95 CI		p
		Lower	Upper		Lower	Upper	
Predicted recurrence-free survival time (month)							
Group 1	98.9	93.1	104.7	-	-	-	***0.005***
Group 2	99.2	93.9	104.5	-	-	-	
Group 3	66.4	57.9	75.0	-	-	-	
Total	93.4	88.1	98.6	-	-	-	
Predicted metastasis-free survival time (month)							
	Mean	% 95 CI		Median	% 95 CI		p
		Lower	Upper		Lower	Upper	
Group 1	92.9	86.9	97.5	-	-	-	***0.017***
Group 2	94.5	86.4	102.5	-	-	-	
Group 3	77.0	63.4	90.6	-	-	-	
Total	90.7	84.7	96.6	-	-	-	
Predicted cancer specific survival time (month)							
	Mean	% 95 CI		Median	% 95 CI		p
		Lower	Upper		Lower	Upper	
Group 1	102.0	102.0	102.0	102.0	-	-	***0.024***
Group 2	94.7	86.8	102.5	-	-	-	
Group 3	79.9	67.2	92.6	-	-	-	
Total	92.2	86.2	98.2	102.0	72.6	131.3	

CI: Confidence interval
Kaplan-Meier (Log-Rank)/The binary difference between the groups was calculated with "Pairwise over strata".

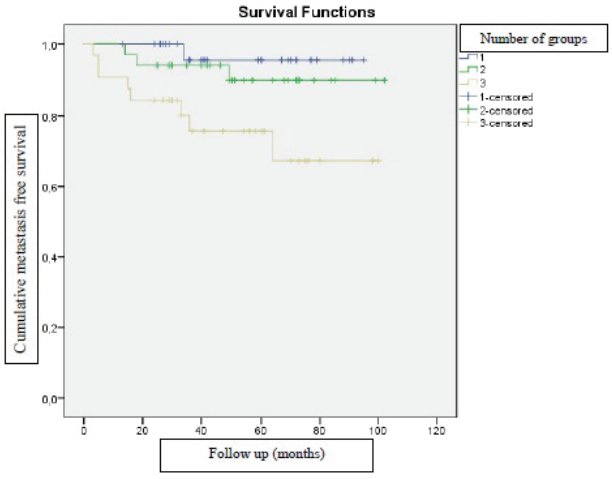

Figure 2. Graph of Kaplan-Meier analysis for predicted metastasis-free survival in three groups

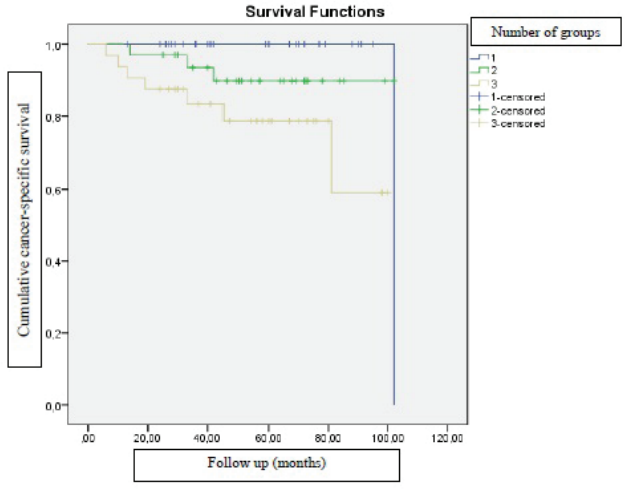

Figure 3. Graph of Kaplan-Meier analysis for predicted cancer-specific survival in three groups

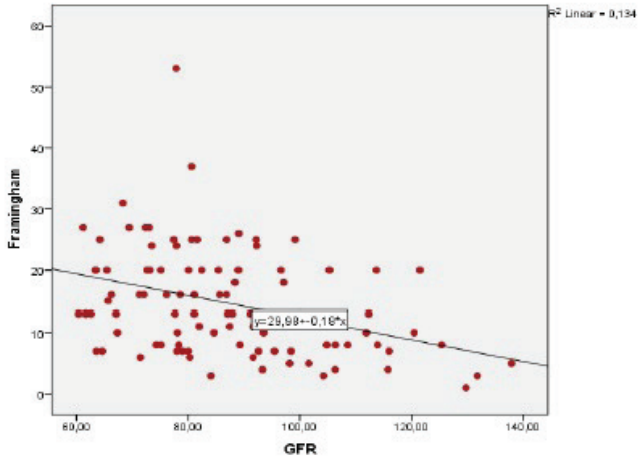

Figure 4. Graphical representation of the correlation between Framingham risk score and eGFR: Estimoted glomenular filtnotion note

survival rates for Fuhrman grades I, II, III, IV were reported as 64%, 34%, 31% and 10%, respectively, and this grading is known to be an important prognostic factor in organ-confined localized disease (22). As a matter of fact, in a multicentre study involving 5009 cases, local recurrence rates at 5 years after nephrectomy were observed as 17.1%, 23.9%, 11.3% and 4.2% for T1a, T1b, T2a and T2b, respectively, during median follow-up of 105 months, and recurrence rates have been reported to be higher in Fuhrman grade 3-4 cases (23).

During a median follow-up of 64 (6-102) months in T1a and T1b patients in our study, local recurrence rates were 9.75% and 14.28%, distant metastasis rates were 9.75% and 25%, and cancer specific survival rates were 92.5% and 86.35%, respectively. Our oncologic results for T1 stage are consistent with current literature data. However, we could not make a significant survival analysis for T2 stage since there were 11 patients and there was no cancer-related mortality during the median 59 (13-99) months follow-up. During the median 57 (6-102) months follow-up of all patients in the T1 and T2 stages, local recurrence was 9.4%, distant metastasis was 12.5%, and cancer-specific survival was 88.5%. Although we observed that Fuhrman grade 3-4 was an independent prognostic factor affecting both local recurrence and cancer-specific survival, we could not find a significant effect on the development of metastasis.

In the literature, there are many studies investigating the effect of metabolic syndrome, including impaired glucose tolerance /diabetes, obesity, high triglyceride levels, low HDL levels and hypertension on oncologic outcomes in RCC (8,9,24). Although there are some contradictory results, metabolic syndrome is thought to be a poor prognostic factor for RCC. It is known that the incidence of RCC increases approximately 4-6 times in patients with three or more metabolic syndrome components (8). It was observed that the tumor size and grade were significantly higher in the presence of metabolic syndrome and that there was a correlation between individual hypertension, diabetes and high triglyceride levels with tumor aggressiveness (9).

Kriegmair et al. (10) showed no significant individual effect of diabetes, obesity (BMI>30 kg/m^2), hypertension and hypertriglyceridemia on progression-free survival (PFS) in localized RCC. However, in the presence of metabolic syndrome consisting of all these components, it was observed that PFS was significantly shortened and cancer-specific survival did not change. When Kocher et al. (11) examined the components of the metabolic syndrome, they found that hypertension has the most significant relationship with high tumor stage, high Fuhrman grade, increased tumor size, increased nephrometry score and non-clear cell histological subtype in RCC.

Eskelinen et al. (12) found a significant relationship between the presence of hypertension and dyslipidemia in patients with local advanced stage RCC at the time of diagnosis and found that, among the metabolic syndrome components, only hypertension was an independent risk factor that increases cancer-related mortality (12). In accordance with these results, another study reported that the presence of type 2 diabetes alone was not found to be a negative prognostic factor for RCC

(25).

When the literature is examined, it is seen that both the presence of metabolic syndrome and the individual components are investigated on the oncologic outcomes in localized RCC. In patients with no required lifestyle changes or medical treatment for blood pressure, lipid profile and body mass index, it is known that they have a risk of developing cardiovascular disease in 10-year follow-up as a result of the cumulative effect of the risk factors. We could not find any study investigating the oncologic outcomes of localized RCC patients classified according to this risk analysis during follow-up after nephrectomy.

Numerous nomograms and risk analyzes are available to estimate the risk of cardiovascular disease, with Framingham Heart Study results affecting most of them (26). The common goal of these risk analyzes is to quantitatively calculate the measurable and preventable risk factors on the development of cardiovascular disease. In this way, it is aimed to determine the appropriate treatment by changing the life style and behavior in the patients at risk.

Smoking, obesity and hypertension are the most important predisposing factors in RCC and are associated with a higher incidence of cancer. Although obesity is known to increase the incidence of RCC, in some studies, better oncologic outcomes have been reported during follow-up after nephrectomy in patients with high BMI (20,27). In our study, although only three patients were in the obese category (BMI ≥30 kg/m^2), we observed that the increase in BMI was associated with more recurrence, distant metastasis and cancer-related mortality, and BMI values were significantly higher in group 3.

Although the number of cigarettes smoked per day and duration of smoking directly affect RCC development, the incidence of RCC decreases by 30% 10 years after smoking cessation (20). In our study, although smoking did not seem to affect oncologic outcomes in univariate and multivariate models, the smoking rate, which is a component of Framingham score, was significantly higher in group 3 where worse prognostic

Table 3. Predictive factors for local recurrence development, distant metastasis development and cancer-specific survival

	Univariate Model				**Multivariate Model**			
Development of local recurrence	HR	%95 CI		**p**	HR	%95 CI		**p**
		Lower	Upper			Lower	Upper	
BMI	1.877	1.381	2.552	***<0.001***	1.779	1.161	2.725	***0.008***
Hypertension	1.118	1.055	1.185	***<0.001***	-	-	-	-
Total cholesterol	1.023	1.009	1.038	***0.001***	-	-	-	-
HDL	0.878	0.774	0.995	***0.042***	-	-	-	-
Fuhrman grade 3-4	3.902	1.560	9.756	***0.004***	5.049	1.388	18.363	***0.014***
eGFR	0.942	0.891	0.995	***0.033***	0.932	0.866	1.003	***0.044***
Framingham risk score	1.192	1.092	1.301	***<0.001***	1.192	1.092	1.235	***<0.001***
	Univariate Model				**Multivariate Model**			
Development of metastasis	HR	%95 CI		**p**	HR	%95 CI		**p**
		Lower	Upper			Lower	Upper	
BMI	1.755	1.364	2.258	***<0.001***	1.755	1.364	2.258	***<0.001***
Hypertension	1.067	1.020	1.117	***0.005***	-	-	-	-
Total cholesterol	1.023	1.010	1.035	***<0.001***	-	-	-	-
eGFR	0.932	0.885	0.981	***0.007***	0.947	0.899	0.998	***0.043***
Framingham risk score	1.125	1.066	1.187	***<0.001***	1.074	0.998	1.156	***0.042***
	Univariate Model				**Multivariate Model**			
Cancer spesific survival	HR Lower	%95 CI		**p**	HR Lower	%95 CI		**p**
		Upper				Upper		
BMI	2.161	1.563	2.989	***<0.001***	2.161	1.563	2.898	***<0.001***
Hypertension	1.076	1.029	1.125	***0.001***	-	-	-	-
Presence of diabetes	3.716	1.055	13.093	***0.041***	-	-	-	-
Total cholesterol	1.019	1.006	1.033	***0.004***	-	-	-	-
Fuhrman grade 3-4	2.788	1.209	6.429	***0.016***	-	-	-	-
eGFR	0.930	0.879	0.984	***0.012***	0.905	0.816	1.003	***0.042***
Framingham risk score	1.139	1.076	1.205	***<0.001***	1.087	1.020	1.159	***0.011***

CI: Confidence interval, HR: Heart rate, BMI: Body mass index, HDL: High-density lipoprotein, eGFR: Estimated glomerular filtration rate
Cox Regression Analysis

outcomes were observed. The incidence of hypertension and diabetes was also significantly higher in this high-risk group.

When all patients in our study were divided into groups according to Framingham risk score, local recurrence rate (21.9%) and distant metastasis rate (25%) were significantly higher, and predicted recurrence-free survival (66.4 months), metastasis-free survival (77 months) and cancer-specific survival (79.9 months) were significantly lower in group 3 with a high risk of developing cardiovascular disease. Although the cancer-specific survival rate was lower (78.1%) in the high-risk group, it was not statistically significant (p=0.059).

As known, partial nephrectomy technique has gained significant role in small renal masses (especially in T1 stage) based on the idea that nephron loss after nephrectomy may increase the course of chronic kidney disease (CKD). An eGFR value of 45-60 mL/min/1.73 m^2, which is the third stage CKD indicator, was observed in 65% after radical nephrectomy and 20% after partial nephrectomy. The rate of severe CKD (eGFR<45 mL/min/1.73 m^2) was 36% after radical nephrectomy and 5% after partial nephrectomy (28). It is known that the decrease in eGFR after nephrectomy leads to an increase in cardiovascular disease and mortality, and a decrease in overall survival (29,30). Ahmedov et al. (20) demonstrated that pre-operatively lower eGFR values also adversely affected cancer-specific survival and recurrence-free survival. In our study, preoperative eGFR was > 60 mL/min/1.73 m^2 in all patients, however, significantly lower eGFR values were found in group 3 with a high risk of cardiovascular disease within 10 years and these patients had worse oncologic outcomes during follow-up. In univariate and multivariate analyzes, we observed that preoperative eGFR level affected local recurrence, metastasis rates and cancer-specific survival. In accordance with these findings, we also showed a significant negative correlation between eGFR and Framingham risk score (r=-0.380, p<0.001). This suggests that relatively lower preoperative eGFR is an independent factor that adversely affects overall survival by increasing both RCC-related mortality and cardiovascular risk.

Limitations of the Study

The retrospective design of our study, the low number of patients, the lack of randomization, and the fact that the follow-up results belong to a single center are the main limiting factors.

Conclusion

In patients with localized-stage RCC who are at high risk of developing cardiovascular disease, more local recurrence, distant metastasis and cancer-related mortality rates can be observed postoperatively despite curative treatment with nephrectomy. Therefore, we suggest that these patients should be followed more carefully in the post-nephrectomy period. The results should be supported with prospective, randomized, multicentre, large-scale studies with longer follow-up periods and the issue should be further clarified.

Ethics

Ethics Committee Approval: Ethical committee approval was not obtained since it is a retrospective study.

Informed Consent: Patients were pre-operatively informed about the use of oncologic follow-up data such as recurrence, metastasis development and survival analysis in various oncological studies without revealing patient names and identity information. The data of patients who did not consent were not used.

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Author Contributions

Surgical and Medical Application: H.B., Concept: H.B., Design: İ.S., Data Collection or Processing: İ.S., Analysis or Interpretation: İ.S., H.B., Literature Search: İ.S., Writing: İ.S.

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