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Pathological Prognostic Features and Analysis of Renal Cell Carcinoma

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ABSTRACT

Renal cell carcinomas is 2-3% of all adult cancers. Kidney cancer is currently the seventh most common cancer in men and the tenth most common in women [1]. There were 19,3 million new cancer diagnoses and 10 million cancer deaths worldwide in 2020 [2].

Survival in renal cell carcinomas has a strong correlation with the stage of diagnosis. 5-year survival in stage 1 tumors is 93%, 72,5% in cases with local lymph node metastases and 12% in metastatic carcinomas cases [3]. There is an inverse correlation between age / tumor size and survival. Metastatic lymph node, tumor necrosis and adipose tissue invasion are associated with poor prognosis [4].

The study is including 179 renal cell carcinoma cases. The clinical and pathological datas of these cases were retrospectively analyzed from the Cumhuriyet University Hospital patient system.

The distribution sex of cases are 111 males (62%) and 68 females (38%). The mean age of the 179 cases was 58,5±11,9 years (range of 21-90). The mean tumor diameter is 5,7±3,4 (range of 1-19 cm). The nuclear grades of cases are 53,1% with low grade and 46,8% with high grade.

Radical nephrectomies were evaluated for vascular invasion, ureter invasion, capsule/adipose tissue invasion, lymph node metastasis and adrenal gland metastasis.

There is a statistically significant relationship between nuclear grade and vein invasion, microvascular invasion, capsule/adipose tissue invasion (p<0,05). Also there is a statistically significant relationship between tumor diameters and vein invasion, microvascular invasion, capsule/adipose tissue invasion, lymph node metastases (p<0,05)

However, there is not a statistically significant relationship between subtypes and vein invasion, micro vascular invasion, capsule/adipose tissue invasion, lymph node metastases, adrenal gland metastases (p>0,05).

It was observed that the invasions increased as the nuclear grade and tumor diameters increased. These observations are statistically significant.

Keywords: Renal cell carcinoma, vascular invasion, nuclear grade, tumor diameters

Renal Hücreli Karsinomun Patolojik Prognostik Özellikleri ve Analizi

ÖZ

Renal hücreli karsinom erişkin yaş grubunda görülen tüm kanserlerin %2-3'ünü oluşturmaktadır. Böbrek kanserleri en sık görülen kanserler arasında kadınlarda onuncu ve erkeklerde yedinci sırada yer almaktadır [1]. 2020 yılında dünya genelinde 10 milyon kanser nedeni ile ölüm ve 19,3 milyon yeni kanser tanısı konulmuştur [2].

Renal hücreli karsinomlarda sağkalımın tanı anındaki evre ile güçlü bir ilişkisi bulunmaktadır. 5 yıllık sağkalım evre 1 tümörlerde %93, lenf nodu metastazı olan vakalarda %72,5 ve metastatik karsinom vakalarında %12'dir. Sağkalım ile yaş ve tümör çapı arasında ters ilişki bulunmaktadır[3]. Metastatik lenf nodu, tümör nekrozu ve çevre yağ doku invazyonu kötü prognoz ile ilişkilidir[4].

Bu çalışmaya 179 renal hücreli karsinom vakası dahil edildi. Cumhuriyet Üniversitesi Hastanesi'nin hasta sisteminden retrospektif olarak klinik ve patolojik veriler tarandı.

Vakaların cinsiyet dağılımı 111(%62)'i erkek ve 68(%38)'i kadın şeklindedir. Vakaların yaş ortalaması 58,5±11,9 (yaş aralığı 21-90) idi. Ortalama tümör çapı 5,7±3,4 (tümör çap aralığı 1-19) idi. Vakaların nükleer derecesi %53,1'inde düşük dereceli %46,8'inde yüksek dereceliydi.

Radikal nefrektomilerde vasküler invazyon, üreter invazyonu, kapsül/yağ doku invazyonu, lenf nodu metastazı ve adrenal gland metastazı değerlendirildi.

İstatistiksel olarak nükleer derece ile ven invazyonu, mikrovasküler invazyon ve kapsül/yağ doku invazyonu arasında anlamlı bir ilişki bulundu (p<0,05). Ayrıca istatistiksel olarak tümör çapı ile ven invazyonu, mikrovasküler invazyonu, kapsül/yağ doku invazyonu ve lenf nodu metastazı arasında anlamlı bir ilişki bulundu (p<0,05).

Ancak, istatistiksel olarak subtipler ile ven invazyonu, mikrovasküler invazyon, kapsül/yağ doku invazyonu, lenf nodu metastazı ve adrenal gland metastazı arasında anlamlı bir ilişki saptanmadı (p>0,05).

Nükleer derece ve tümör çapları arttıkça invazyonların arttığı saptandı. Bu bulgular istatistiksel olarak da anlamlı bulundu.

Anahtar sözcükler: Renal hücreli karsinom, vasküler invazyon, nükleer derece, tümör çapı

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Introduction

Renal cell carcinoma (RCC), originating from the epithelium of the renal tubulus, is the most common malignant tumor of the kidney. These tumors are 2-3% of all adult cancers. There were 19,3 million new cancer diagnoses and 10 million cancer deaths worldwide in 2020. Kidney cancer is currently the seventh most common cancer in men and the tenth most common in women. 1,8% of cancer deaths are caused by kidney cancers [1,2]. The incidence of kidney tumors has increased according to the data of the Turkish Ministry of Health. While kidney cancer was the seventh most common cancer in 2002, it was the fifth most common cancer in 2016 in men (5).

RCC is mostly diagnosed between the ages of 65 and 74. Clear cell renal cell carcinoma (CCRCC) is the most common type RCC and papillary renal cell carcinoma (PRCC) is the second most common type RCC [3,5]. Chromophobe renal cell carcinoma (ChRCC) accounts for 4-6% of all RCC and has a better prognosis [5,6]. PRCC is more common in patients over 60 years than CCRCC. ChRCC is not associated with age [7].

Most RCCs develop sporadically but about 2-4% are familial. It is about twice as common in men than in women. Renal cell carcinoma is very rare in children [5]. According to some studies the etiology of renal cell carcinoma includes smoking, hypertension and high body mass index.

Nuclear grading of RCC is also considered a prognostic factor. The grading for grades 1-3 is based on nucleolar prominence/eosinophilia, while nuclear anaplasia (sarcomatoid differentiation) is required for grade 4 [8,9,10].

Moreover, survival in kidney tumors has a strong correlation with the stage at the time of diagnosis. 5-year survival in stage1 tumors is 93%, 72,5% in cases with local lymph node metastases and 12% in metastatic carcinomas cases [3]. There is an inverse correlation between age/tumor size and survival [11]. Metastatic lymph node, tumor necrosis and adipose tissue invasion are associated with poor prognosis [4,12].

Material-Method

The population of this descriptive, cross-sectional study consists of 179 patients diagnosed with RCC in Sivas Cumhuriyet University Hospital Pathology Department between 2017 and 2022. No sample selection was made and all patients diagnosed with RCC were included in the study.

Primarily, it was classified according to the demographic characteristics (age, sex) of the patients.

Patients diagnosed with renal cell carcinoma were distributed according to the subtypes of the disease (CCRCC, PRCC, ChRCC), and the nuclear grade of the disease was grouped as low (1-2 grade) and high (3-4 grade). Tumor diameters of the patients were examined in 3 groups (1st group with 1-6 cm, 2nd group with 7-13 cm, 3rd group with 14-19 cm).

The types of operations that the patients had undergone were evaluated as radical and partial, on the right and left kidneys of the operation side. In radical nephrectomies cases, the relationship between nuclear grade, tumor diameters, subtypes and vein invasion, microvascular invasion, capsule/ adipose tissue invasion, lymph node metastases, adrenal gland metastates was analyzed as statistically.

SPSS-22 (SPSS INC., Chicago, IL, USA) statistical program was used in the analysis of the data. While count data was give in with numbers and percentages, measurement data was givein with mean, standard deviation, minimum and maximum values. The nominal data were compared with the chi-square test. The findings obtained by statistical analysis are presented with descriptive and analytical tables.

Results

The distribution sex of total 179 cases are 111 males (62%) and 68 females (38%). Radical nephrectomy was performed in 112 cases (62,6%) and partial nephrectomy was performed 67 cases (37,4%). The tumors were located in the left kidney of 81(45,3%) cases and in the right kidney of 98(54,7%) cases. The mean age of the 179 cases was 58,5±11,9 years (range of 21-90). The mean tumor diameter is 5,7±3,4 (range of 1-19 cm) (Table I).

Histopathological subtypes were CCRCC in 141 cases (78,8%), PRCC in 27 cases (15,1%) and ChRCC in 11 cases (6,1%). Sarcomatoid differentiation was observed in 10 cases (5,6%). Nuclear grades were evuluated in 158 cases; grade1 6,3% (n=10), grade2 46,8% (n=74), grade3 27.2% (n=43) and grade4 19,6% (n=31) (Table I). The median age is 58 in CCRCC cases, 62 in PRCC cases and 55 in ChRCC cases.

Nuclear grade and tumor diameter were compared with vein invasion, capsule/adipose tissue invasion, microvascular invasion, lymph node metastasis and adrenal gland metastasis. Nuclear grades 1 and 2 were defined as low grade, grades 3 and 4 as high grade. Tumor diameters of 1-6 cm were defined as group 1, 7-13 cm as group 2 and 14-19 cm as group 3.

Table I. The age, sex, nuclear grade, tumor diameter, operation and diagnosis distribution of cases

		n	%	Mean±Std Dev	Min – Max
Age				58. 5 ± 11.9	21 – 90
Tumor diameter (cm)				5.7 ± 3.4	1 – 19
Sex					
	Female	68	38.0		
	Male	111	62.0		
Location					
	Right	98	54.7		
	Left	81	45.3		
Operation					
	Radical	112	62.6		
	Partial	67	37.4		
Diagnosis					
	CCRCC	141	78.8		
	PRCC	27	15.1		
	ChRCC	11	6.1		
Nuclear grade					
	Grade 1	10	6.3		
	Grade 2	74	46.8		
	Grade 3	43	24.0		
	Grade 4	31	19.6		

Only surgical margin was evaluated in partial nephrectomies. Surgical margin evaluated in 61 cases was positive in 4 cases and negative in 57 cases (Table II).

Table II. Surgical margin evaluation in partial nephrectomy cases

		n	%
Surgical margin	Positive	4	6.5
	Negative	57	93.5

Tablo III. Comparison of nuclear grade and invasions, metastases in radical nephrectomy cases

		Low Grade		High Grade		
		n	%	n	%	p
Vein invasion	Positive	5	11,3	20	35,7	**0,005**
	Negative	39	88,7	36	64,3	
Microvascular invasion	Positive	3	13,6	17	54,8	**0,005**
	Negative	19	86,4	14	45,2	
Capsule/adipose tissue invasion	Positive	1	2,3	11	19,6	**0,010**
	Negative	41	97,7	45	80,4	
Lymph node metastases	Positive	0	0,0	2	40,0	0,357
	Negative	4	100,0	3	60,0	
Adrenal gland metastases	Positive	1	33,3	1	7,6	0,054
	Negative	2	66,7	12	92,4	

There was vein invasion for 5 cases in low grade, for 20 cases in high grade. There is a statistically significant relationship between grade and vein invasion (p=0,005). There was microvascular invasion for 3 cases in low grade, for 17 cases in high grade. There is a statistically significant relationship between grade and micro vascular invasion (p=0,005). There was capsule/adipose tissue invasion for a case in low grade, for 11 cases in high grade. There is a statistically significant relationship between grade and capsule/adipose tissue invasion (p=0,010). 2 cases with high grade had lymph node metastases. There is not a statistically significant relationship between grade and lymph node metastases (p=0,357). Of the 2 cases with adrenal gland metastases, one was low grade and the other was high grade. There is not a statistically significant relationship between grade and adrenal gland metastases (p=0,054) (Table III).

Table IV. Comparison of tumor diameter and invasions, metastases in radical nephrectomy cases

		Group1		Group2		Group3		
		n	%	n	%	n	%	p
Vein invasion	Positive	8	12.9	15	34.8	4	66.6	**0.001**
	Negative	54	87.1	28	65.2	2	33.4	
Microvascular invasion	Positive	7	28.0	10	45.4	4	66.6	**0.008**
	Negative	18	72.0	12	54.6	2	33.4	
Capsule/adipose tissue invasion	Positive	1	1.6	7	17.5	5	83.4	**0.000**
	Negative	60	98.4	33	82.5	1	16.6	
Lymph node metastases	Positive	0	0.0	1	33.3	2	66.7	**0.000**
	Negative	3	100.0	2	66.7	1	33.3	
Adrenal gland metastases	Positive	0	0.0	1	14.2	1	100.0	0.053
	Negative	8	100.0	6	85.8	0	0.0	

There was vein invasion for 8 cases in group 1, for 15 cases in group 2 and for 4 cases in group 3. There is a statistically significant relationship between tumor diameters and vein invasion (p=0,001). There was microvascular invasion for 7 cases in group 1, for 10 cases in group 2 and for 4 cases in group 3. There is a statistically significant relationship between tumor diameters and microvascular invasion (p=0,008). There was capsule/adipose tissue invasion for a case in group 1, for 7 cases in group 2 and for 5 cases in group 3. There is a statistically significant relationship between tumor diameters and capsule/adipose tissue invasion (p=0,00). There was no lymph node metastases in group 1, while there was for a case in group 2 and for 2 cases in group 3. There is a statistically significant relationship between tumor diameters and lymph node metastases (p=0,00). There was no adrenal gland metastases in group 1, while there was for a case in group 2 and for a case in group 3. There is not a statistically significant relationship between tumor diameters and adrenal gland metastases (p=0,053) (Table IV).

Table V. Comparison of subtypes and invasions, metastases in radical nephrectomy cases

		CCRCC		PRCC		ChRCC		
		n	%	n	%	n	%	p
Vein invasion	Positive	24	26,6	2	12,5	1	16,6	0.431
	Negative	66	73,4	14	87,5	5	83,4	
Microvascular invasion	Positive	19	42,4	1	12,5	1	33,3	0,630
	Negative	26	57,8	7	87,5	2	66,7	
Capsule/adipose tissue invasion	Positive	12	13,6	0	0,0	1	16,6	0,500
	Negative	76	86,4	15	100,0	5	83,4	
Lymph node metastases	Positive	2	25,0	0	0,0	1	25,0	0,255
	Negative	6	75,0	1	100,0	3	75,0	
Adrenal gland metastases	Positive	2	15,3	0	0,0	0	0,0	0,750
	Negative	11	84,7	3	100,0	0	0,0	

There is not a statistically significant relationship between subtypes and vein invasion, microvascular invasion, capsule/adipose tissue invasion, lymph node metastases, adrenal gland metastases (Table V).

Discussion

Renal cell carcinomas is 80-85% of all primary malignant tumors of kidney and it is 2-3% of all adult cancers. Renal cell carcinoma is mostly diagnosed between the ages of 65 and 74 [1,2]. In this study, the mean age was 58,5±11,9 years (range of 21-90). It is about twice as common in male as in female (-[4]. Our data were compatible with the literature (female 38%, male 62%).

PRCC in patients over 60 years of age is more common than CCRCC. ChRCC is not associated with age and has a better prognosis [3,13]. The mean age is 58 in CCRCC cases, 62 in PRCC cases and 55 in ChRCC cases.

The mean age was higher in PRCC cases which was consistent with the literature.

CCRCC is the most common subtype and PRCC is the second most common subtype in RCC. ChRCC accounts for 4-6% of all RCC [4]. Diagnosis of cases were 78,8% CCRCC, 15,1% PRCC and 6,1% ChRCC in this study.

The incidence of renal cell carcinomas has increased in recent years. It is known that the prognosis of RCC depends on nuclear grade, tumor diameters, age and invasions. One study was shown lymphovascular invasion and microvascular invasion are poor prognostic factors in RCC [9,14].

In RCCs, nuclear grade and tumor diameter are correlated with tumor stage and help in determining the prognosis. In this study, it was found that the increasing in nuclear grade and tumor diameter are associated with poor prognostic factors. There are also studies that have achieved similar results in the literature [11,12].

Conclusion

In conclusion, there is a statistically significant relationship between nuclear grade and vein invasion, microvascular invasion, capsule/adipose tissue invasion in this study. In addition, there is a statistically significant relationship between tumor diameters and vein invasion, microvascular invasion, capsule/adipose tissue invasion, lymph node metastases.

Disclosure statement

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

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