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How Competent is Computed Tomography in Characterization and Grading of Renal Malignancies: Our Experience

Böbrek Malignitelerini Karakterizasyon ve Derecelemede Bilgisayarlı Tomografi Ne Kadar Yetkin: Bizim Deneyimimiz

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Abstract

Objectives: Accurate diagnosis of renal tumors is critical for obtaining the best treatment and longest possible survival. The purpose of this study is to evaluate computed tomography (CT) parameters of renal masses in order to assess benign and malignant nature as well as accurate grading.
Materials and Methods: Fifty three cases with multiphasic abdominal CTs between 2006 and 2011 were included. Precontrast, corticomedullary, nephrographic postcontrast phase images were retrospectively examined for lesion characteristics, enhancement degrees with regard to the normal renal parenchyma and abdominal aorta, blinded to the surgical results.
To compare independent groups for categorical variables chi-square, for metric variables Mann-Whitney U tests were used. Receiver operating characteristics curve analysis was performed to group renal tumor subtypes and when applicable the cut-off values were determined, "Youden" index was calculated. $p<0.05$ was considered as statistically significant.
Results: Forty six of 53 lesions were malignant, 32 (57.1%) of them clear cell renal cell carcinomas (CCRCC), 5 (9.4%) papillary and 1 (1.9% chromophobe cell RCC. Cystic changes, calcifications and larger size were more pronounced in CCRCC ($p< 0.05$). The mean sizes of Fuhrman grade I and grade 4 tumors were 31.2±10.9 mm and 63.8±29.8 mm respectively. Fuhrman grades were significantly correlated with the lesion size at diagnosis ($p<0.05$).
To discriminate CCRCC from other masses and CCRCC from other RCC subtypes, 44.5 HU cut-off as the early wash-in showed 81.3%-76.2 % and 81.3%-87.5% sensitivity and specificity, respectively.
To discriminate CCRCC among other subtypes the threshold levels calculated from early wash-in, tumor/aorta, tumor/renal parenchyma densities at corticomedullary and nephrographic phases showed equal sensitivity and specificity (83.5% and 75% respectively).
Conclusion: Large size at diagnosis, cystic changes and calcifications were useful parameters to discriminate CCRCC from other tumors and other RCC subtypes. A cut- off value of 44.5 HU for early wash-in could discriminate CCRCC with high sensitivity and specificity. Size and cystic changes showed significant correlation with RCC subtypes and Fuhrman grades.
Key Words: Kidney, Renal Cell Carcinoma, Multiphasic Computed Tomography, Clear Cell Variant

Öz

Giriş: Uygun tedavi ve mümkün olan en uzun sağkalım için böbrek tümörlerinde doğru tanı kritik önem taşır. Bu çalışmanın amacı böbrek kitlelerinde benign-malign ayrımı ve doğru dereceleme için bilgisayarlı tomografi (BT) parametrelerinin ayrıntılı incelenmesidir.
Gereç ve Yöntem: Çalışmaya 2006-2011 yılları arasında ünitemizde multifazik BT incelemesi gerçekleştirilmiş 53 hasta dahil edilmiştir. Prekontrast, kortikomedüller ve nefrografik faz görüntülerinde kitle, normal parankim ve abdominal aorta kontrastlanma dereceleri ile lezyonların görüntüleme bulguları, retrospektif ve cerrahi sonuçlara kör olarak değerlendirilmiştir. İstatistiksel analizde bağımsız gruplarda kategorik değişkenler için ki-kare, ölçülebilir değişkenler için Mann-Whitney U testi, kullanılmış, renal tümör tiplerini ayırmada alıcı işletim karakteristiği eğirisi analizleri gerçekleştirilmiştir, uygun parametrelerde eşik değer belirlemede "Youden" indeksi hesaplanmıştır. $p<0,05$ istatistiksel olarak anlamlı kabul edilmiştir.
Bulgular: Elli üç lezyondan 46 tanesi malign olup bunların 32'si (%57,1) berrak hücreli renal karsinom (BHRK), 5'i (%9,4) papiller ve 1 tanesi

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(%1,9) kromofob hücreli renal karsinomdu. İntralezyoner kistik değişiklikler, kalsifikasyonlar ve büyük boyut BHRK'de daha fazlaydı (p<0,05). Furhman derece 1 tümörlerde ortama boyut 31,2±10,9 mm iken, derece 4 tümörlerde 63,8±29,8 mm olarak saptandı. Tanı anındaki kitle boyutları ile Fuhrman dereceleri arasında anlamlı ilişki gözlendi (p<0,05). Erken wash-in eşik değeri olarak 44,5 HÜ alındığında BHRK'leri diğer renal kitlelerden ve diğer renal karsinom alt tiplerinden ayırmada duyarlılık ve özgüllük değerleri sırasıyla %81,3-%76,2 ile %81,3-%87,5 olarak bulundu. Tüm renal karsinomlar arasında BHRK'lerin ayrımı için bakılan parametrelerden elde edilen eşik değerlerine göre erken wash-in, kortikomedüller ve nefrografik fazlarda tümör/ aorta ve tümör/ normal renal parankim dansite oranları eş duyarlılık ve özgüllükte bulundu (sırasıyla; %83,5 ve %75).
Sonuç: Tanıda büyük boyut, kistik değişiklikler ve kalsifikasyon BHRK'leri diğer renal kitelerden ve diğer renal karsinom alt tiplerinden ayırmada kullanışlı parametreler olarak bulundu. Ayrıca erken wash-in eşik değeri olarak 44,5 HÜ alındığında BHRK'ların yüksek duyarlılık ve özgüllükle doğru tespit edilebileceği saptandı. Büyük boyut ve intralezyoner kistik değişiklikler, BHRK alt tipi ve yüksek Fuhrman derecesi ile korele bulundu.
Anahtar Kelimeler: Böbrek, Renal Hücreli Karsinom, Mulifazik Bilgisayarlı Tomografi, Berrak Hücreli Variant

Introduction

Correct diagnosis of renal masses is crucial for determining the best course of treatment and longest possible survival of the patient. With the recent innovations in computerized tomography (CT) technologies, CT is a widely used diagnostic modality which yields high quality preoperative information about renal masses such as size, anatomic relationship to crucial structures, as well as their nature and prognosis. The purpose of this study was to evaluate multiple parameters of renal lesions in order to characterize any given renal mass initially as benign or malignant and derive a correct subtype diagnosis depending on CT findings. The evaluated parameters include lesion size, CT findings of local invasiveness and degree of enhancement. A thorough study on lesion enhancement has been conducted. Fuhrman grades of renal cell carcinomas (RCC) were correlated with CT findings.

Materials and Methods

Patients

Between years 2006 and 2011, 62 patients with solid renal lesion were examined of whom 53 were included in the study and 9 were excluded due to lack of surgical correlation.

The study design is in accordance with ethical standards of the World Medical Association (Declaration of Helsinki).

Image Acquisition

All patients were examined by multi-detector row computed tomography. Two patients were examined with an eight-detector row scanner (light Speed Ultra; General Electric Healthcare, Milwaukee, USA) and 51 patients were examined by a 64-detector row scanner (Aquilion, Toshiba Medical Systems, Japan)

100 mL nonionic contrast medium was injected through an antecubital vein catheter at a rate of 2-3 mL/s by an automatic injector. The CT protocol included a precontrast scan of upper abdomen (from the dome of diaphragm to the level of iliac crests), followed by postcontrast images for corticomedullary phase (CMP) with a delay of 40 seconds and nephrographic phase (NGP) with a delay of 100 seconds of the same region.

Scan parameters were tube voltage 120 kV, tube current 300 mA, collimation 8x1.25 mm, and a pitch of 0.75 for the eight-detector row CT, and collimation 64x0.5 mm, rotation time 0.5 seconds, a pitch of 0.83 for the 64-detector row CT.

Reconstructed slice thickness and reconstruction interval were 1.25 mm/0.5 mm and 0.5/0.5 mm for the eight and 64-detector row scanners, matrix was 512 x 512.

Image Analysis

Two radiologists, blinded to the tissue diagnoses retrospectively reviewed the images at dedicated workstations (Advantage Windows 4.0, GE Healthcare and Vitrea 4.0). Precontrast, corticomedullary and nephrographic phase attenuation measurements of the lesions were performed with a region of interest. From these measurements CT densities at each phase, early and late wash-in (enhancement) values were calculated as follows:

The mean values of at least three separate regions of interest (ROI) were recorded. For substantially heterogenous solid masses the ROI cursors were carefully placed at the most enhancing part of the mass and for cystic lesions, measurements were taken from the thick septa or solid components. The same location of the lesion with the same size of ROI cursor was used at all three phases of the examination. Areas of calcification and cystic spaces were avoided during the measurements.

Early wash-in: CMP lesion attenuation-precontrast lesion attenuation

Late wash-in: NGP lesion attenuation-precontrast lesion attentuation.

Normal renal parenchymal attenuation was measured from a clearly non-tumoral region of the ipsilateral kidney. Aortic attenuation was measured at the level of renal artery orifices. For both CMP and NGP, the ratio of tumor attenuation to normal parenchymal attenuation (tumor/parancyhme attenuation ratio), and the ratio of tumor attenuation to aortic attenuation (tumor/aorta attenuation ratio) were calculated.

Additionally, general lesion morphology (cystic and calcific changes) were noted when present. The data on postoperative pathology results of tumor type, and for renal cell carcinoma cases, the Fuhrman grade, tumor subtype and information about renal capsule and perirenal fat invasion were collected retrospectively from the hospital's information system.

Statistical Analysis

Statistical analyses were performed by SPSS 11.5 and MedCalc. Mean ± standard deviation [median (minimum-maximum)] for metric variables, frequency (percent) for categorical variables was used as descriptive statistics. For the comparison of two independent groups, chi-square test was used for categorical variables, Mann-Whitney U test was used for metric variables. In order to determine the sign and magnitude of relationships between metric variables, Spearman correlation coefficient was calculated.

For the evaluation of metric values to discriminate renal cell carcinomas from other renal masses and clear cell subtype receiver operating characteristics (ROC) curve analysis was conducted. When the area under the ROC- curve was statistically significant, this parameter could be used to discriminate the analyzed groups from each other. In order to determine the cut-off values for appropriate parameters, "Youden" index (Sensitivity + Specificity -1) was calculated. P<0.05 was considered as statistically significant.

Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of CT findings for the stage of renal tumors were calculated.

Results

Among the 53 patients, 28 were males and 25 were females. Mean [± standard deviation (SD)] age of the patients was 58.1 (±15.7) years (ranging from 3-86 years) and the male to female ratio was 1.2:1.

Mean (± SD) tumor diameter in the axial plane was 45.6 (±25.3) mm (ranging from 10 to 116 mm). The pathologic diagnosis of the smallest (10 mm) and the largest (116 mm) tumors in this study were both clear cell type RCC. For clear cell RCC and non-clear cell RCC groups the mean (± SD) sizes were 47.4 (±24) mm and 50.5 (±28.1) mm respectively and there was no statistical significance between these groups with respect to tumor size (p>0.05).

Seven of the 53 lesions were benign and 46 were malignant. The two non-epithelial malignant tumors in this study were 1 case of (1.9%) malignant mesenchymal tumor and 1 case of (1.9%) mixed epithelial stromal tumor. There was 1 case of (1.9%) non-tumoral renal infarct extending into the perinephric fat (Table 1).

The presence of cystic changes was not statistically significant to discriminate lesions as benign and malignant (Figure 1) (p>0.05). However, cystic changes were significantly more frequent in clear cell RCCs (23 cases) (p<0.05).

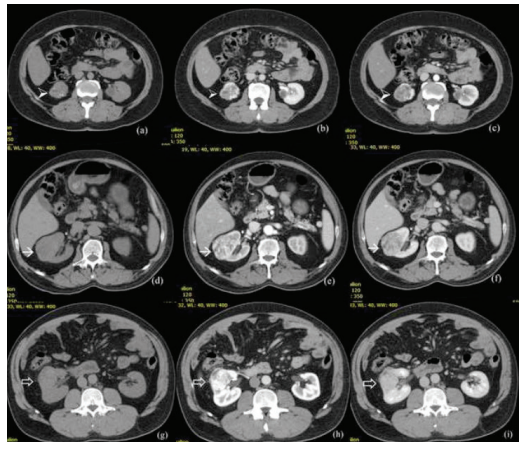

Figure 1: Note the three different right renal masses with similar CT appearances in precontrast, corticomedullary and nephrographic phases respectively

(a), (b) and (c) represent a mass (arrow-head) in a 45-year-old female patient. Note the punctate calcifications and small cystic areas in this lesion. Radiologically mistaken as a renal cell carcinoma (RCC), this lesion was diagnosed as mixed epithelial stromal tumor after surgery. Note the similarity of CT images of this lesion with the right renal mass (arrow) in (d), (e) and (f), depicting a grade 1 clear cell RCC in an 80-year-old male. The lesion in (g), (h), (i) also contains punctate calcifications and small cystic spaces, representing a grade 3 clear cell RCC in a 50 year old male.

Table 1: Distribution of cases with regard to histopathological diagnosis, and presence of cystic changes and calcification

Histopathological diagnosis	Number of lesions (%)	Cystic changes present (%)	Calcifications present (%)
Clear cell RCC	32 (60.4%)	23 (43.4%)	1 (1.9%)
Papillary RCC	5 (9.4%)	0	0
Transitional cell carcinoma	4 (7.5%)	2 (3.8%)	0
Collecting duct type RCC	2 (3.8%)	1 (1.9%)	0
Lipid poor angiomyolipoma	2 (3.8%)	1 (1.9%)	0
Oncocytoma	2 (3.8%)	1 (1.9%)	0
Chromophobe cell RCC	1 (1.9%)	0	0
Wilms tumor	1 (1.9%)	0	1 (1.9%)
Metanephric adenoma	1 (1.9%)	0	0
Non-epithelial tumors	2 (3.8%)	2 (3.8%)	2 (3.8%)
Non-neoplastic lesions	1 (1.9%)	0	0
Total	53 (100%)	30 (56.6%)	4 (7.5%)

RCC: Renal cell carcinoma

Intralesional calcification was encountered in only 7.5% of the lesions (Table 1). Presence of calcification was not predictive of the tumor type, or the malignancy or benignity of the mass (p>0.05).

CT Attenuations, Wash-in Values, Tumor/Aorta Attenuation Ratios and Tumor/Parenchyma Attenuation Ratios

Table 2 shows the attenuation characteristics of clear cell RCCs versus all other renal lesions. The precontrast attenuation of clear cell RCCs were not significantly different from all other renal lesions, however clear cell RCCs showed significantly higher corticomedullary and nephrographic phase attenuation, early wash-in and late wash-in than all other lesions (p<0.05). They also had higher tumor/aorta and tumor/parenchyma attenuation ratio in both corticomedullary and nephrographic phases (p<0.05).

Table 3 shows the attenuation characteristics of clear cell RCCs versus non-clear cell RCCs. The precontrast attenuation of clear cell RCCs was significantly lower than that of non-clear cell RCCs. Clear cell RCCs displayed significantly higher corticomedullary and nephrographic phase attenuation, early and late wash-in than non-clear cell RCCs. They also showed higher tumor/aorta and tumor/parenchyma attenuation ratios in both corticomedullary and nephrographic phases than non-clear cell RCCs.

Table 2: Attenuation characteristics of clear cell carcinomas versus other renal lesions

		Precon (HU*)	CMP (HU)	NGP (HU)	EW (HU)	LW (HU)	Tm/ aorta CMP	Tm/ aorta NGP	Tm/paren CMP	Tm/paren NGP
Total (n=53)	Mean	30.8	108.7	84.5	77.9	53.3	0.34	0.55	0.54	0.39
	SD	6.7	61.9	29.5	63	30.4	0.29	0.31	0.42	0.24
CC-RCC (n=32)	Mean	29.7	130	93.9	100.2	63.4	0.45	0.66	0.70	0.47
	SD	5.9	63.6	29.5	64.5	30.5	0.30	0.30	0.43	0.24
Other lesions (n=21)	Mean	32.4	76.3	70.2	43.9	37.9	0.18	0.37	0.29	0.25
	SD	7.6	43.2	23.7	43.1	23.3	0.16	0.22	0.28	0.17
	p	**0.089**	**0.001**	**0.006**	**0.001**	**0.003**	**<0.001**	**<0.001**	**<0.001**	**0.001**

(*HU: Hounsfield units)
Precon: Precontrast, CMP: Corticomedullary phase, NGP: Nephrographic phase, EW: Early wash-in, LW: Late wash-in, Tm/aorta: Tumor/aorta attenuation, Tm/paren: Tumor/parenchyma attenuation, CC-RCC: Clear cell renal cell carcinoma, SD: Standard deviation

Table 3: Attenuation characteristics of clear cell carcinomasversus non-clear cell (papillary, collecting duct and chromophobe cell) carcinomas

		Precon (HU*)	CMP (HU)	NGP (HU)	EW (HU)	LW (HU)	Tm/aorta CMP	Tm/aorta NGP	Tm/paren CMP	Tm/paren NGP
Total (n=40)	Mean	30.6	117.3	88	86.6	56.8	0.39	0.59	0.61	0.42
	SD	6.2	63.8	29.7	65	30.9	0.30	0.31	0.43	0.24
CC- RCC (n=32)	Mean	29.7	130	93.9	100.2	63.4	0.44	0.66	0.70	0.47
	SD	5.9	63.6	29.5	64.5	30.5	0.30	0.30	0.43	0.24
Non-clear cell RCC (n=8)	Mean	34	66.3	64.5	32.3	30.5	0.15	0.32	0.23	0.21
	SD	6.2	32.1	16.7	29.1	15.1	0.12	0.18	0.18	0.10
	p	**0.036**	**0.005**	**0.013**	**0.003**	**0.005**	**0.003**	**0.002**	**0.001**	**0.002**

(*HU: Hounsfield units)
Precon: Precontrast, CMP: Corticomedullary phase, NGP: Nephrographic phase, EW: Early wash-in, LW: Late wash-in, Tm/aorta: Tumor/aorta attenuation, Tm/paren: Tumor/parenchyma attenuation, CC-RCC: Clear cell renal cell carcinoma, SD: Standard deviation

Table 4. The distribution of RCC lesions with respect to the Fuhrman grades

Fuhrman grades	Grade 1	Grade 2	Grade 3	Grade 4	Total number
Clear cell RCC	5 (12.5%)	15 (37.5%)	8 (25%)	4 (12.5%)	32 (80%)
Papillary RCC	1 (2.5%)	2 (5%)	2 (5%)	0	5(12.5%)
Chromophobe RCC	0	1(2.5%)	0	0	1(2.5%)
Collecting duct RCC	0	0	0	2 (2.5%)	2 (5%)
All	6 (15%)	18 (45%)	10 (25%)	6 (15%)	40 (100%)

RCC: Renal cell carcinoma

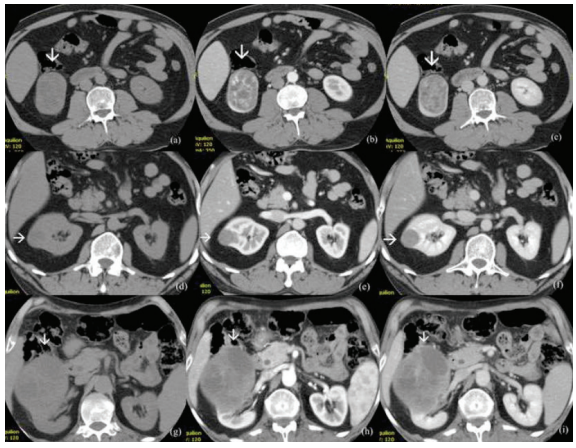

Figure 2: Precontrast, corticomedullary and nephrographic phase images of clear cell (arrows) (a-c), papillary cell (arrows) (d-f) and chromophobe cell (arrows) (g-i) renal carcinoma The clear cell and papillary RCCs were Fuhrman grade 1 and chromophobe RCC was a Fuhrman grade 2 lesion. Note the relatively less enhancement of papillary RCC and heterogeneity and larger size of the high grade chromophobe RCC.

Table 5: Lesion size with respect to Fuhrman grade

Fuhrman grade	Mean diameter (mm) ± SD	Median (mm) (minimum-maximum)
Grade 1	31.2±10.9	34.5 (10-40)
Grade 2	45.9±22	40 (20-110)
Grade 3	52.5±27.3	47.5 (26-116)
Grade 4	63.8±29.8	59 (30-115)
All grades	48±24.5	40 (10-116)

SD: Standard deviation

Fuhrman Grades of RCC Lesions

The Fuhrman grades of all RCC cases according to subtypes are summarized in Table 4.

Table 5 shows the relationship between the lesion size and Fuhrman grade. The larger carcinomas had significantly higher Fuhrman grade than the smaller ones (Figure 2) ($p<0.05$).

Results of ROC-Curve Analyses

Table 6 shows the sensitivity and specificity of different attenuation parameters for differentiating the clear cell RCCs from all other lesions. Area under ROC curve was not statistically significant for any of the attenuation parameters so that a reliable threshold could not be obtained for discriminating malignant from benign masses. Table 7 shows the sensitivity and specificity

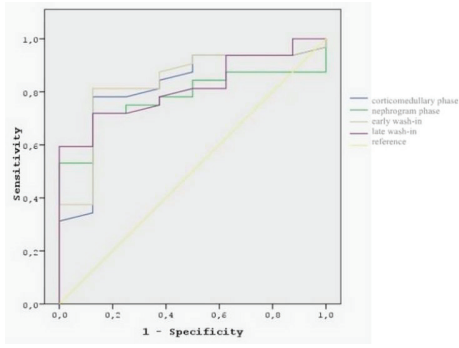

Figure 3: This ROC curve compares corticomedullary, nephrographic phase attenuations, early and late wash-in values for discrimination of clear cell RCCs from non-clear cell RCCs.

Table 6: Sensitivity and specificity of various attenuation parameters in discriminating clear cell RCCs from all other lesions

Clear cell RCC vs all lesions	Precon.	CMP	NGP	EW	LW	Tm/aorta d-CMP	Tm/aorta d-NGP	Tm/paren. d-CMP	Tm/paren. d-NGP
Area under ROC curve	0.639	0.760	0.726	0.769	0.745	0.787	0.788	0.793	0.783
p- value	0.089	0.001	0.006	0.001	0.003	<0.001	<0.001	<0.001	<0.001
Cut-off (HU)	-	82.5	83	44.5	43.5	0.26	0.415	0.315	0.315
Sensitivity (%)	-	78.1	71.9	81.3	71.9	78	81.3	81.3	72
Specificity (%)	-	76.2	71.4	76.2	71.4	76.2	71.4	71.4	71

Precon: Precontrast, CMP: Corticomedullary phase, NGP: Nephrographic phase, EW: Early wash-in, LW: Late wash-in, Tm/aorta: Tumor/aorta attenuation, Tm/paren: Tumor/parenchyma attenuation, ROC: Receiver operating characteristics, HU: Hounsfield units

Table 7: Sensitivity and specificity of various attenuation parameters in discriminating clear cell renal cell carcinomas from non-clear cell renal cell carcinomas

Clear cell RCC vs non-clear cell RCC	Precon.	CMP	NGP	EW	LW	Tm/aorta d-CMP	Tm/aorta d-NGP	Tm/paren. d-CMP	Tm/paren. d-NGP
Area under ROC curve	0.740	0.816	0.781	0.832	0.816	0.830	0.846	0.850	0.846
P	0.038	0.006	0.015	0.004	0.006	0.004	0.003	0.002	0.003
Cut- off (HU)	33.5*	82.5	83	44.5	43.5	0.185	0.415	0.315	0.245
Sensitivity (%)	81	78	71.9	81.3	71.9	81.3	81.3	81.3	81.3
Specificity (%)	63	88	87.5	87.5	87.5	75	87.5	87.5	75

Precon: Precontrast, CMP: Corticomedullary phase, NGP: Nephrographic phase, EW: Early wash-in, LW: Late wash-in, Tm/aorta: Tumor/aorta attenuation, Tm/paren: Tumor/parenchyma attenuation, ROC: Receiver operating characteristics

of different attenuation parameters for differentiating the clear cell RCCs from non-clear cell RCCs. Clear cell and non-clear cell RCCs have an inverse relationship with respect to precontrast densities.

Figure 3 exemplifies the comparison of ROC curves obtained for CMP, NGP densities early and late wash-in values for discrimination of clear cell RCCs versus non-clear cell RCCs.

Statistically significant correlations could not be achieved between attenuation parameters and Fuhrman grades of the all RCC lesions (n=40), the clear cell subtypes (n=32) or papillary subtypes (n=5).

Discussion

Renal cell carcinoma is by far the most common malignant renal tumor. The incidence tends to increase after the age of 40, making up almost 2% of all adult cancers worldwide, 3.7% of all new cancer cases, mainly in the developed countries with 2-3 times higher prevalence in males (1-3). Between 1974 and 1990, a 38% increase in the incidence of renal cell carcinoma has been detected, whereas only a 5% increase in the five year survival could be accomplished. Both of these rises in incidence are due to the increased success rates at the diagnosis of this tumor (4).

In the recent years, with the development of targeted therapies, survival rates are expected to increase. As a result the role of radiologic evaluation is gaining more importance in the follow up of the patients in addition to its main role of accurate diagnosis (5).

For diagnosis, in CT studies, an increase in a renal lesion density by 10- 20 HU after contrast administration is considered as a sign of solid nature (6-8). In our study, we considered a 20 HU increment as a cut- off.

A renal mass smaller than 4 cm in diameter at initial diagnosis is more likely to be benign (9,10). Birnbaum et al. (10) reported that tumor grade correlates better with CT findings in small renal carcinomas. Our study has supported this finding and we found that larger tumors at the initial diagnosis tend to have higher grades.

There were no correlations between the enhancement parameters of the clear cell and papillary RCCs and their Fuhrman grades, so tumor size was found to be the most helpful parameter at predicting differentiation level.

It is also known that tumor subtype is at least as important as the tumor grade for prognosis. According to the Heidelberg classification in 1997, clear cell RCC accounts for the 65% of all renal cortical masses, 70-80% of all renal cell carcinomas and 90% of all metastatic cases (8,11,12). Papillary and chromophobe subtypes, on the other hand, account for only 25% of all renal tumors and 10% of renal tumor metastases. Consequently, the five year survival rate with these tumors is much higher (80-90%), compared to the clear cell variant (50-60%) (13). Additionally it is found that histologic subtype of RCC also determined the metastatic pattern and the sites of involvement. Being able to correctly identify clear cell type RCCs by preoperative CT is therefore critical (14,15). In the present study, it has been shown that discrimination of clear cell RCC among other solid renal tumors could be accomplished with both morphological and attenuation parameter analyses, which can help predict the patient prognosis. Cystic changes were significantly more common in clear cell variant (43.4%) and not present in any of the papillary or chromophobe subtypes.

We found that CMP and NGP attenuation, early and late wash- in values, tumor/aorta and tumor/parenchyma attenuation ratios were all statistically significant parameters in differentiating clear cell carcinomas from other renal tumors and among different renal carcinoma subtypes. Previous studies have mentioned the importance of CMP of the multiphasic CT examinations (16-18). In the present study a CMP attenuation cut-off of 82.5 HU could reliably differentiate clear cell renal carcinomas from other RCC subtypes with 78.1% sensitivity and 76.2% specificity. This is very close to 83.5 HU found by Sheir et al. (16). However we found that an early wash-in cut off value of 44.5 HU, which was derived from the CMP density, had the highest sensitivity and specificity to differentiate clear cell RCCs from all other solid renal lesions (81.3/ 76.2% respectively) as well as to differentiate clear cell RCCs from other RCC subtypes (83.1%, 87.5% respectively).

For subgrouping RCC types, although all the parameters were useful, paradoxically a lower precontrast lesion density indicated clear cell subtype. We think this finding is due to the more compact cellular structure of papillary and chromophobe types. Also the presence of more cystic changes within the tumor in clear cell variant may be another factor.

Other researchers have reported varying degrees of enhancements at post-contrast series (10,16). We calculated the tumor/aorta and tumor/parenchyma density ratios in order to avoid such conflicts due to differences in contrast injection parameters or factors like renal vein thrombosis which could result in compromised ipsilateral renal enhancement. These ratios were slightly more sensitive (81%) compared to CMP densities (78%). Diagnostic sensitivity could be increased from 71.9% to 81% to discriminate clear cell RCCs among all RCCs, when the ratio threshold of 0.245 is used instead of NGP threshold of 83HU.

Young et al. (19) found that both the peak enhancement and enhancement at CMP of clear cell RCCs were significantly greater than oncocytomas, however in our study, none of the attenuation parameters proved to be a reliable cut-off to distinguish malignant from benign renal masses. This is probably due to the limited number of benign lesions particularly oncocytomas (only 2 cases) in our study.

Although calcific or cystic change was not predictive of malignancy or benignity, cystic change strongly indicated the clear cell type in malignant masses, which was in accordance with the findings of Sheir et al. (16). Contrary to our results, calcification has been shown to have a role in estimating the subtype of RCCs by Kim et al. (20).

Study Limitations

Our study has several limitations. The retrospective design of the study and small sample size are the major limitations. For the renal carcinoma subtypes of collecting duct and chromophobe cell RCCs, there were not adequate number of cases for statistical comparison. Also the numbers of other benign and some malignant renal tumors were low so they could not be individually assessed. Because of the relatively small number of less frequent RCC subtypes and benign solid renal lesions, further studies with larger sample sizes are required to compare each type and subtype of renal tumor.

Conclusion

Discriminating benign enhancing renal lesions from malignant ones by the help of CT is still problematic so patients with benign renal lesions continue to undergo unnecessary surgeries. However, we found that once a renal lesion is considered to belong to the malignant category, certain CT findings and measurements can aid in the recognition of clear cell variant of RCCs from the others. An early wash-in index of 44.5 HU was determined to guide the radiologist towards clear cell type with high sensitivity and specificity. A large tumor size at initial diagnosis and presence of cystic changes within the lesion imply both a high Fuhrman grade and clear cell subtype.

Ethics

Ethics Committee Approval: Retrospective study.

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: Z.A., C.Y., Design: Z.A., C.Y., Data Collection or Processing: Z.A., C.Y., Analysis or Interpretation: Z.A., D.G., Literature Search: Z.A., E.P., A.G.Ç., Writing: Z.A.

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