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Characterization of Small Renal Masses Less than 4 cm with Quadriphasic Multidetector Helical Computed Tomography: Differentiation of Benign and Malignant Lesions

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Purpose: To identify the characteristic quadriphasic (unenhanced, corticomedullary, nephrographic, and excretory phase) helical multidetector computed tomography (MDCT) features of renal masses less than 4 cm to distinguish benign from malignant renal masses.

Materials and Methods: In total, 84 patients were retrospectively analyzed to determine the characteristic features for the prediction of subtypes of small renal masses. The patients' age, gender, and tumor size and CT features, including the presence of intra-tumor degenerative changes, septation, calcification, and wall irregularity, were evaluated. In addition, the degree and pattern of enhancement obtained during four phases were analyzed. The relationship between the subtype of the small renal masses and the gender, morphological features, and pattern of contrast enhancement on the CT was analyzed by using the chi-square test. Tumor size and degree of contrast enhancement were compared by the Mann-Whitney U test. The predictive value of each of the CT features was determined by multivariate logistic regression analysis.

Results: Of the 84 small renal masses, 17 (20%) were benign and 67 (80%) were malignant. Univariate analysis revealed that renal cell carcinoma lesions showed heterogeneous enhancement (p=0.002) and higher mean attenuation value on the corticomedullary and nephrographic phases (135.1±53.9, p=0.000, and 132.4±43.6, p=0.006). The multivariate analysis with logistic regression model showed that only the mean attenuation value on the corticomedullary phase had a statistically significant correlation (p=0.021).

Conclusions: For the characterization of small renal masses, the degree of enhancement on the corticomedullary phase is a valuable parameter. Furthermore, the heterogeneous enhancement pattern and degree of enhancement on the nephrographic phase can provide information for differentiating small renal masses.

Key Words: *Benign neoplasm; Computed tomography; Renal cell carcinoma*

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INTRODUCTION

With the widespread use of cross-sectional imaging modalities, an unprecedented number of incidental small renal masses have been identified. Although simple cysts account for the majority of these lesions, there are also a large number of malignancies. Therefore, differentiation of benign from malignant lesions has become an important issue.

Computed tomography (CT) remains the most useful imaging modality for the assessment of renal masses; CT provides an accurate evaluation of tumor size, location, organ confinement, status of the tumor wall, and margin irregularity. Helical multidetector CT (MDCT) has sig-

nificantly improved the imaging of renal masses by decreasing respiratory misregistration and allowing rapid volumetric data acquisition free of skip areas. Furthermore, MDCT has expanded multiphasic scanning capabilities while at the same time providing superior axial resolution and multiplanar reformation options with very thin collimation. This technology might allow for the analysis of the degree and pattern of dynamic contrast enhancement from identical levels in the kidney at each phase [1]. Therefore, previously undetectable or indeterminate findings with conventional CT are better characterized by MDCT.

Some studies have been carried out to differentiate between small benign renal masses and malignancies less than 4 cm in diameter by use of MDCT. For instance, renal oncocytomas, which are benign tumors, might be treated conservatively if a definitive noninvasive diagnosis can be made. Some literature has reported features of MDCT that can differentiate oncocytomas from renal cell carcinomas (RCCs) [2,3]. However, no definite criteria have been established.

Our aim was to identify the characteristic quadriphasic [unenhanced, corticomedullary (CMP), nephrographic (NP), and excretory phase (EP)] helical MDCT features of small renal masses less than 4 cm to distinguish benign from malignant renal masses.

MATERIALS AND METHODS

1. Patient selection

We performed a retrospective review of the medical records and diagnostic imaging studies of 84 patients with pathologically confirmed solitary renal masses 4 cm or less in diameter. All patients had either open or laparoscopic removal of a presumed unilateral, unifocal RCC at our institution between 2000 and 2009. All lesions were thought to be RCC on preoperative imaging as evaluated by an experienced genitourinary radiologist who was unaware of the surgical and histological findings. All patients had four-phase scans that were consecutively acquired by helical MDCT. The patients known preoperatively to have non-RCC lesions on CT, such as angiomyolipoma (AML), transitional cell carcinoma, or a benign nonfunctioning kidney, were excluded. No patient had a known history of von Hippel-Lindau disease, contralateral nephrectomy for RCC, or synchronous bilateral RCC.

2. MDCT scanning

All CT examinations were performed by using a helical CT scanner (GE Medical Systems LLC, Milwaukee, WI, USA). All patients had four-phase CT imaging that included an unenhanced scan before administration of intravenous contrast material injection and the evaluation of the CMP, NP, and EP after contrast material injection, which is the standard spiral CT protocol at our medical center. The CT protocol remained constant and consisted of volumetric data acquisition of the kidney using 5-mm thin collimation, a 0.5-s gantry rotation speed, a tube voltage of 120 kV, and a tube current of 200 to 240 mAs; table feed, 7 mm/s; and reconstruction interval, 3 mm.

All patients received 150 ml of intravenous contrast material (iopromide, Ultravist 300, Bayer Schering Pharma, Berlin, Germany) by use of a dynamic bolus technique (injection into an antecubital vein by use of a power injector at a rate of 3.0 ml/s). The delay was 30 seconds for the CMP, 70 seconds for the NP, and 180 seconds for the EP.

3. Image analysis

Axial and reformatted images were evaluated for the presence or absence of calcification within the lesion, attenuation on the unenhanced scans, degenerative changes, septation, and margin irregularity. For evaluation of the degree of enhancement, strict measurement of the attenuation value was performed by use of a standard elliptic cursor for the region of interest, placed in the center of the most enhanced solid portion, which was consistent in location during all phases of the MDCT and compared with that of the unenhanced scan. Precontrast attenuation was determined by visual inspection and was classified as hypo-attenuation, iso-attenuation, and hyper-attenuation by comparison with the attenuation of the surrounding renal parenchyma. We considered the tumor to be hyperattenuating when the difference in density was positive and greater than 10 HU, hypoattenuating when the difference was negative but still greater than 10 HU, and isoattenuating when the difference was less than 10 HU.

The degree of enhancement of each phase was measured by calculating the difference in the mean attenuation value between the CMP and the unenhanced scan, the NP and the unenhanced scan, and the EP and the unenhanced scan, respectively.

The enhancement pattern was classified as homogeneous when most of the tumor areas showed a uniform degree of enhancement on both the CMP and the NP. The enhancement pattern was classified as heterogeneous in the remaining cases.

4. Pathology examination and analysis

Histological sections were reviewed by consensus of two experienced pathologists using a double-headed light microscope simultaneously. The histopathologic findings were reviewed for the subtype of neoplasm, the presence of intra-tumor necrosis or hemorrhage, and the existence of septation.

5. Statistical methods

Statistical analysis was performed with SPSS ver. 12.0 (SPSS, Chicago, IL, USA). The relationship between the subtype of the small renal masses and the gender, morphological features, and pattern of contrast enhancement on the CT was analyzed by using the chi-square test. Tumor size and degree of contrast enhancement were compared by the Mann-Whitney U test. To assess the predictive value of various characteristics observed on the MDCT that sig-

TABLE 1. Patient demographic and clinical data

	Benign	Malignant	p-value
No. of patients (%)	17 (20)	67 (80)	
Age (yr)	61.3±13.9	63.2±11.5	0.680
Male/Female, no. (%)	7/10 (41/59)	50/17 (75/25)	0.002
Renal mass			
Pathology, no. (%)	AML 6 (35) Oncocytoma 8 (47) Cortical adenoma 2 (12) Infected cyst 1 (6)	Clear cell RCC 57 (85) Papillary RCC 4 (6) Chromophobe RCC 5 (7) Collecting duct RCC 1 (2)	
Size (cm)	2.41±0.73	2.74±0.65	0.072
Laterality (right/left), no. (%)	7/10 (41/59)	33/34 (49/51)	0.551
Contour, no. (%)			
Exophytic	9 (53)	44 (66)	0.331
Endophytic	8 (47)	23 (34)	
Location, no. (%)			
Upper pole	6 (35)	22 (33)	
Mid pole	4 (24)	24 (36)	0.741
Lower pole	7 (41)	21 (31)	

Values are presented as number (%) or mean±SD.
AML, angiomyolipoma; RCC, renal cell carcinoma.

nificantly differentiated RCC from benign renal masses, multivariate logistic regression analysis was performed. To evaluate the diagnostic efficacy of the degree of enhancement during the various phases of enhancement, receiver operating characteristic (ROC) curves were generated. The curves were analyzed to determine the cutoff value during four phases for differentiating malignancies from small benign renal masses with the highest accuracy. p-values of less than 0.05 were regarded as statistically significant.

RESULTS

1. Descriptive analysis

The mean patient age was 63.2±11.5 years (range, 32 to 83 years) in the patients with RCC and 61.3±13.9 years (range, 31 to 75 years) in those with benign lesions ($p > 0.05$). The male-to-female ratio was 2.9:1 for the patients with RCC and 0.7:1 for the patients with benign lesions (p=0.002). The mean diameter of the renal masses, obtained from the preoperative MDCT, was 2.74±0.68 cm (range, 1 to 4 cm) for RCC and 2.41±0.73 cm (range, 1.5 to 3.8 cm) for benign lesions ($p > 0.05$). On the basis of the pathology reports, of the 84 small renal masses, 17 (20%) were benign and 67 (80%) were malignant. The benign lesions consisted of eight oncocytomas, six AML, two cortical adenomas, and one infected mass. The 67 RCCs were of the following subtypes: 57 (85%) clear cell, 4 (6%) papillary, 5 (8%) chromophobe, and 1 (1%) collecting duct. A histopathology examination of the small RCCs revealed that 44 tumors were mostly grade 1 and grade 2 (66%); 22 (33%) tumors were grade 3, and 1 was grade 4. The demographic information was not significantly different between the benign and malignant small renal masses, except for gender (Table 1).

TABLE 2. MDCT features of small renal masses

	Benign (n=17)	Malignant (n=67)	p-value
Calcification, no. (%)	0	6 (9)	
Cystic degeneration, no. (%)	0	17 (25)	
Septation, no. (%)	0	7 (10)	
Wall irregularity, no. (%)	0	5 (8)	
Attenuation in NEC, no. (%)			
Hypoattenuation	1 (6)	8 (12)	
Isoattenuation	15 (88)	51 (76)	1.000
Hyperattenuation	1 (6)	8 (12)	
Enhancement pattern, no. (%)			
Homogeneous	14 (82)	25 (37)	0.002
Heterogeneous	3 (18)	42 (63)	
Hounsfield unit			
HU at NEC	32.58±7.82	29.58±10.59	0.122
HU at CMP	92.88±41.18	135.16±53.90	0.000
HU at NP	89.47±42.40	132.49±43.64	0.006
HU at EP	90.17±33.52	102.29±31.44	0.071

Values are presented as number (%) or mean±SD.
MDCT, multidetector computed tomography; HU, Hounsfield unit; NEC, nonenhanced CT; CMP, corticomedullary phase; NP, nephrographic phase; EP, excretory phase.

2. Morphologic features on the MDCT

Cystic degeneration, calcification, septation, and wall irregularity showed only in cases with RCC. Table 2 summa-

TABLE 3. Multivariate analysis with logistic regression model

	p-value	Exp (B)	95% CI for EXP (B)	
			Lower	Upper
Sex	0.017	5.156	1.347	19.737
Enhancement pattern	0.055	0.265	0.068	1.027
HU CMP	0.021	0.975	0.954	0.996
HU NP	0.519	1.009	0.982	1.037

CI, confidence interval; HU, Hounsfield unit; CMP, corticomedullary phase; NP, nephrographic phase.

rizes a comparison between the features of benign and malignant lesions.

3. Pattern and degree of contrast enhancement

The 67 RCCs had a mean attenuation value of 29.5±10.5 HU on the unenhanced scan (range, 5 to 50 HU). All carcinomas showed significant contrast enhancement (more than 20 HU) after intravenous injection of contrast [mean enhancement during CMP: 135.1±53.9 HU [range, 47 to 288 HU]; mean enhancement during NP, 132.4±43.6 HU [range, 62 to 273 HU]; mean enhancement during EP: 102.2±31.4 HU (range, 36 to 201)]. On the other hand, benign renal masses showed less contrast enhancement; mean enhancement was less than 100 HU during all MDCT phases [during CMP: 92.8±41.1 HU (range, 54 to 143); during NP: 99.3± 42.4 HU (range, 68 to 229); during EP: 89.4±33.5 HU (range, 44 to 180)]. Overall, the mean attenuation value on the CMP and the NP was significantly higher in cases with RCC than in benign lesions (Table 2).

The peak phase enhancement was different for each histopathological subtype of the small renal masses. Most of the clear cell types of RCC (60%) showed a peak enhancement on the CMP; however, all cases of AML and six of eight cases of oncocytoma showed gradual enhancement with a peak attenuation value on the NP. For the traditional MDCT criteria for lesion characterization, namely, the morphologic features and the pattern and degree of contrast attenuation of the lesion, the multivariate analysis with logistic regression model showed that only the mean attenuation value on the CMP had a statistically significant correlation; this was found whether the lesions were benign or malignant (p=0.021) (Table 3).

Combining the gender and mean attenuation value on the CMP showed 94% sensitivity, 41% specificity, 86% positive predictive value, and 64% negative predictive value.

The ROC curve analysis showed that the cutoff value with the highest accuracy for characterization of small renal masses was 87 HU on the CMP and 73 HU on the NP. The area under the curve for the CMP was 0.785 (95% confidence interval: 0.667-0.902), and that for the NP was 0.717 (95% confidence interval: 0.579-0.854) (Fig. 1).

Although all except three benign renal masses (two oncocytomas, one AML) showed homogeneous enhancement during all phases of the MDCT, 41 out of 67 (61%) RCC lesions showed heterogeneous enhancement; the differences were statistically significant (p=0.002).

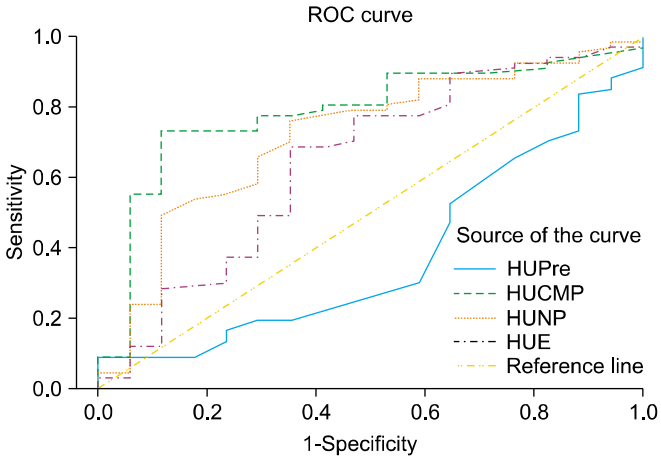

FIG. 1. Receiver operating characteristic (ROC) curves for the degree of contrast enhancement as a distinguishing factor between small malignant masses and small benign masses. The area under the curve for the corticomedullary phase (CMP) was 0.785 (95% confidence interval [CI], 0.667 to 0.902), which was statistically significant, and that for the nephrographic phase (NP) was 0.717 (95% CI, 0.579 to 0.854). CMP, corticomedullary phase; NP, nephrographic phase.

DISCUSSION

Renal parenchymal tumors are a very heterogeneous group of lesions, ranging from benign to highly aggressive. Accordingly, the morphologic features and the degree and pattern of enhancement vary significantly depending on the architecture and subtype of the tumor; the findings show a considerable amount of overlap. Therefore, the characterization of renal parenchymal tumors by use of imaging modalities can pose considerable difficulties.

The precise preoperative prediction of the histological type of lesion may be helpful not only for determining the appropriate treatment plan, such as the extent of the preoperative evaluation and surgery, but also in counseling the patient preoperatively.

To improve the detection and characterization of renal parenchymal tumors, a dedicated quadriphasic MDCT protocol was used in this study. The images obtained only during the CMP phase failed to identify many of the small renal masses that were easily seen on the NP [4,5].

Although as in other studies [6,7], RCC was the most common lesion, in this series, 67 (80%) out of 84 small renal masses less than 4 cm in diameter (a significant fraction of small solitary renal masses that were presumed to be RCC) had a benign final pathology. The overall rate of benign tumors was 20% in this group of patients. These results are consistent with previously published reports that 16 to 27% of small renal masses less than 4 cm are likely to be benign [8-10].

In this series, the male-to-female ratio was 2.9:1, which was statistically significant. This finding is consistent with previously published reports of a male-to-female predominance of 3:2 [11].

Furthermore, in this study, the attenuation value was the most useful parameter for differentiating small renal masses, especially on the CMP. RCC showed strong enhancement, regardless of the subtype, during the three phases of imaging after contrast injection. In addition, RCC showed a more heterogeneous enhancement, whereas most of the benign small renal masses showed homogeneous enhancement.

The findings of prior studies are consistent with the results of this study. A study reported by Kim et al. [12] showed that RCC had strong enhancement on biphasic CT, with a contrast enhancement of over 100 HU on the CMP, at 115±48 HU, compared with the level of enhancement on the EP, at 62±25. Jinzaki et al. [13] compared the degree and pattern of contrast enhancement on the CMP and late NP with the findings of 40 renal neoplasms smaller than 3.5 cm. All clear cell types of RCCs exhibited a peak attenuation value on the CMP of more than 100 HU (165.0±45.8 HU), which was significantly higher than among the other renal tumors.

Renal oncocytoma is a benign tumor that develops in the proximal tubular epithelium. Choudhary et al. [14] reported that 18 (64%) of 28 patients with renal oncocytoma showed significant enhancement of the tumor, isodense to the renal cortex, whereas 10 (36%) lesions were hypodense to the surrounding renal cortex in the nephrographic phase with 20 HU or more. Furthermore, although large oncocytomas can exhibit a central stellate scar on the CT, it was found in only three (10%) lesions, all of which were larger than 4 cm in this study. These CT findings were nonspecific and might or might not be observed in RCCs and therefore cannot be used as a determinant of the subtypes of renal tumors. Davidson et al. [15] also reported that most renal oncocytomas smaller than 3 cm showed homogeneous enhancement on all sections of contrast-enhanced CT without a central stellate scar. By contrast, RCCs less than 3 cm in diameter showed that half of the small RCCs had homogeneous contrast enhancement with a hypoattenuating lesion, suggestive of necrosis. Therefore, CT features, such as homogeneous enhancement and a central stellate scar, were poor predictors of the diagnosis of oncocytoma. Bird et al. [3] investigated enhancement and washout values obtained by MDCT to distinguish oncocytoma from RCC in tumors <4 cm. This study demonstrated that CMP enhancement greater than 500% and washout values of greater than 50% are exclusively seen in renal oncocytomas.

In the case of AML, it is composed of various amounts of mature adipose tissue, smooth muscle, and thick-walled abnormal vessels. The presence of intra-tumor fat on the MDCT, measuring less than -30 HU on the unenhanced scan, is indicative of an AML [16,17]. Therefore, if sufficient fat is present on macroscopic detection, most AMLs, even when quite small, can be diagnosed readily by MDCT. However, AMLs with minimal fat may have undetectable fat on CT or magnetic resonance imaging. This makes them difficult to differentiate from RCCs [18,19]. Six cases of AML in this study may also have had minimal fat. This explains why an experienced genitourinary radiologist thought them to be RCC on preoperative imaging of these lesions.

The limitations of this study include the following. The enhancement pattern could vary according to contrast injection variables and scan delay times. Therefore, the threshold value we have reported is applicable only to patients with similar contrast injection protocols and scan delay times. This was a retrospective study. In addition, the number of benign small renal masses was relatively small for the analysis of the MDCT features that differentiate malignancies from benign masses. Because of the small number of renal masses, this study did not evaluate differences of each subtype of RCC. This is due to the low frequency of radiologically indeterminate or suspected malignant lesions. In most cases, the mass is confirmed as benign by pathology due to the accuracy of the helical MDCT with optimized kidney scan protocol and thin collimation with multiphasic volumetric data acquisition. Therefore, further investigations with a much larger number of cases will be necessary in the future.

CONCLUSIONS

For the characterization of small renal mass, the degree of enhancement on the CMP is the most valuable parameter. Furthermore, the heterogeneous enhancement pattern and degree of enhancement on the NP can provide information for differentiating small renal masses from malignancies. This could aid in decisions about treatment by differentiating malignant tumors, which require surgical intervention, from benign lesions, which may be adequately managed by conservative treatment.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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