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The analysis of multiple CT features of renal clear cell carcinoma and the value

KEYWORDS: renal clear cell carcinoma; imaging features; diagnosis

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ABSTRACT **Objective** To investigate the multiple CT features of renal clear cell carcinoma (CCC) and determine their clinical value. **Methods** CT imaging features of 39 patients with renal CCC confirmed by pathology were retrospectively analyzed, and their diagnostic value were also evaluated including the size, shape, location, rim, calcification, necrosis, arteriovenous malformation, metastasis and the enhanced patterns, degrees and curves. The relationships between the imaging findings were also analyzed. **Results** The large size of the tumor was associated with the irregular shape, involving at least two portions of kidney, necrosis, type III of enhanced curve and arteriovenous malformation (P <0.05). The hyper-vascular CCCs were related with the lesions with more necrosis, heterogeneous enhancement and type I and II of enhanced curves (P <0.05). Meanwhile, the lesions with unclear rim were likely with type I and II of enhanced curves (P <0.05), and the regular lesions were likely without arteriovenous malformation (P <0.05). Moreover, the metastasis was related to the lesion with heterogeneous enhancement and necrosis (P <0.05). **Conclusion** CT is an effective imaging modality in the diagnosis and assessment of renal clear cell carcinoma, which may provide accurate information for prognosis estimation of therapeutic effect.

Introduction

Renal cell carcinoma (referred to as kidney cancer) is a common retroperitoneal malignant tumour accounting for 90% of renal tumours and 2% of all malignancies in adults originating from renal tubular epithelium(1). Among all the renal cell carcinomas, clear cell carcinoma (CCC) is the most common subtype (also known as common or conventional renal cell carcinoma) representing between 70% and 75% of all the renal cell carcinomas. Other pathological subtypes of renal cell carcinoma includes, papillary carcinoma, chromophobe cell carcinoma, polycholesteroleucule renal cell carcinoma and so on(2). Around 90% of the clear cell carcinomas tend to be sporadic while about 5% appears to be involved with hereditary syndromes such as von Hippel Lindau disease, tuberous sclerosis(3).

The origin of CCC is from proximal convoluted tubule of the kidney which is pathologically defined as a renal cortical tumour. It is characterized by malignant epithelial cells including a clear cytoplasm, a compact alveolar or aciner growth pattern and arborizing vasculature(4,5). Renal CCC rich in blood supply trends to metastasis usually with a low patient's 5-year survival rate. Therefore, accurate diagnosis of CCC is very important for the treatment and prognosis(6-8). According to the American college of Radiology, MDCT of the abdomen is regarded as a standard technique for detecting and staging of small or incidentally detected renal tumours (≤ 3cm in diameter). When there is a contraindication for CECT, further application of MRI is appropriate(9). It is important to identify some typical CT features of CCC such as hypervascularity, heterogeneity, necrosis, hemorrhage, and liquefaction. Usually a CCC under CT scan presents with hypodensity in precontrast scan, intense contrast uptake in corticomedullary phase and washout in nephrographic phase. Many other features such as unclear border, irregular shape, and rare calcification were also observed. Some other atypical features were observed including hyperdensity-isodensity-hypodensity in precontrast scan whereas hypodensity, clear border, regular shape, and little necrosis with many calcification in postcontrast scan. We here retrospectively analyzed some CT imaging features of 39 patients with renal CCC confirmed by pathology in order to evaluate the value of CT in the diagnosis of renal CCC and improve the diagnostic accuracy.

Materials and Methods

Patients and lesions

We collected retrospectively the patients in our hospital from March 2013 to September 2016 who were scanned by pre- and post-contrast CT and diagnosed as tumor, followed by nephrectomy and histopathologically diagnosed as CCC. And 39 patients (16 women and 23 man, mean age 54.6±12,0 yrs, range from 26-77 yrs) were enrolled in the study including 21 tumors in right kidney and 18 in the left.

CT Scanning

CT Examination: Patients were scanned by a CT scanner (GE Discovery 750 HD, GE Healthcare, USA) in supine position and holding their breath during scanning. All patients received preoperative plain CT and triphasic contrast-enhanced CT examination. The scanning parameters were as follows: ganty rotation time: 0.33 s, tube potential: 100 kVp, effective tube current: 100 mA, pitch: 1.2, collimation: 32 mm ×0.6 mm, beam collimation: 64 mm. The contrast media (Ultravist with the iodine concentration of 300 mg / ml, 1.5 ml/kg, Bayer Pharma, German) was injected into the dorsal vein with a power injector at a flow rate of 3 ml/s, and the

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CT images in arterial, venous, and delayed phase were received respectively.

Image analysis

All the CT images were reviewed independently by two experienced radiologists. Different parameter of tumour were under consideration such as size, shape, enhancement patterns, degrees and curves, vascularity, location, contour of tumor (clear or unclear), metastasis, necrosis and arteriovenous malformation. We measured the size of tumor in centimeter, and then classified them into large (>3 cm) and small size (≤3 cm). The shape was considered as either regular mass or irregular one. Necrotic area in mass was observed in arterial,venous and delayed phases. Location types of mass were in right or left kidney, or in cortex or medulla, or in upper, middle, lower pole or mixed type (involved more than two poles). Enhancement degrees of the mass were classified into type 1 (iso-attenuation), 2 (hypo-attenuation) and 3 (hyper-attenuation) according to the differences in the enhanced degrees between the mass and the cortex. For heterogeneous lesions, the radiologist selected the area to measure the CT value that demonstrated the greatest degree of enhancement of the renal lesion in the arterial phase. Regions of interest (ROI) of measurement were placed in the lesion without necrosis and bleeding and in the adjacent normal renal cortex and aorta. Iso- and hyper-attenuation of the lesion was regarded as hyper-vascularity, meanwhile the hypo-attenuation was hypo-vascularity. In addition, three enhanced curves were also defined as type I (rapid wash-in and wash-out of the contrast in the lesion) , II (rapid wash-in, then platform and rapid wash-out) and III (slow wash-in and wash-out). Calcification or artifacts area were also evaluated Some correlations of the features of the mass with imaging presence were probed. All data were analyzed using a software package (SPSS 17.1) for the statistical analysis including t-test, ANOVA and Pearson correlation analysis.

Results

The CT manifestations of renal CCC

In the study, we found mean size of all lesions was 5.08±3.57 with the size range from 1.1cm to 19.9cm. On plain CT, 3 lesions with hemorrhage and other 3 lesions with calcification were found. Post-contrast CT showed only 2 lesions were located at the cortex, 33 at medulla and 4 at both cortex and medulla; 7 lesions at upper portion of the kidney, 15 at middle part, 9 at lower part and 8 at both upper and lower portions. The post-contrast CT also revealed 12 with clear rim and other 27 with unclear rim in arterial phase, 14 with clear rim and other 25 with unclear rim in venous phase, and 17 with clear rim and other 22 with unclear rim in delayed phase. 34 lesions was round and other 5 was irregular in shape. In terms of the enhanced patterns, CT showed 17 homogeneous lesions and 22 heterogeneous ones in arterial or venous phase, and 23 homogeneous lesions and 16 heterogeneous ones in delayed phase (Fig.1-3). Meanwhile, the arteriovenous malformation around 5 lesions was found in arterial and venous phases. As for the enhanced degrees of the lesions, the hypo-, iso- and hyper-dense lesions in arterial phase were 8, 10 and 21 respectively which indicated 31 hyper-vascular lesions and 8 hypo-vascular ones, those in venous phase were 26, 4 and 9, and in delayed phase were 38, 1 and 0 (Fig.1-3). In addition, The lesions with type I, II and III of enhanced curve were 21, 14 and 4, respectively. Moreover, we also found 24 lesion with necrosis but other 15 without it, and 5 patients with metastasis but other 34 patients without it.

The correlations between the various CT characteristics

As for the relation between lesion size and other evaluated parameters, we found the large size of the tumor was associated with the irregular shape, involving two portions of kidney at least, necrosis, type III of enhanced curve and arteriovenous malformation (P <0.05) (Table 1). In terms of the relationships between the vascularity types of the lesion and other parameters, we found the hyper-vascular CCCs were closely related with the lesions with more necrosis, heterogeneous enhancement and type I and II of enhanced curves (P <0.05) (Table 2). Meanwhile, the number of renal CCCs with type I, II and II of enhanced curves which had clear rim was 9, 4 and 4 respectively, and those which had unclear rim was 12, 10 and 0 respectively, exhibiting a significant difference (P=0.039, x2=6.465) . In addition, the regular and irregular lesions without arteriovenous malformation were 34 and 2 respectively, meanwhile those with arteriovenous malformation were 0 and 3 respectively, also exhibiting a significant difference (P=0.001, x2=22). Moreover, the metastasis was related to the lesion with heterogeneous enhancement and necrosis (P <0.05) (Table 3). However, we did not found the relations between other CT evaluated parameters (P>0.05).

TABLE 1: Relationships between the lesion sizes and other evaluated parameters

	Shape		Necrosis in Arterial phase		Necrosis in venous phase		Necrosis in delayed phase		Arteriovenous malformation		Enhancement Curve			Location 3			
	Round	Irregular	(+)	(-)	(+)	(-)	(+)	(-)	(+)	(-)	Type 1	Type2	Type3	Upper	Middle	Lower	Mixed
Size (cm)	4.63±3.27	8.18±4.35	6.09±4.06	3.47±1.71	6.57±4.28	3.52±1.60	6.79±4.27	3.46±1.55	10.57±3.80	4.63±3.19	4.44±1.86	5.01±3.72	8.73±7.58	3.90±1.92	4.11±1.73	3.43±1.45	9.79±5.02
P(t)	0.036 (2.182)		0.024 (2.358)		0.006 (2.988)		0.004 (3.212)		0.004 (3.064)		0.085 (2.645)			0.002 (7.235)			

TABLE 2: Relationships between the vascularity types of the lesion and other related parameters

	Necrosis		Enhanced patterns		Enhanced curve types		
	(-)	(+)	Homogeneity	Heterogeneity	I	II	III
Hypo-vascularity	6	2	6	2	3	2	3
Hyper-vascularity	9	22	11	20	18	12	1
P (X2)	0.037 (5.677)		0.044 (4.38)		0.027 (8.116)		

TABLE 3: Relationships between the metastasis of the lesion and other related parameters

Metastasis	Enhanced patterns		Necrosis	
	Homogeneity	Heterogeneity	(-)	(+)
Non	22	12	15	20
Yes	0	5	0	4
P (x^2)	0.047 (4.692)		0.047 (4.692)	

3 Discussion

Renal clear cell carcinoma is a common renal cell carcinoma with a higher degree of malignancy. According to the 2004 WHO published renal histological analysis, there are renal CCC, chromophobe cell carcinoma, papillary carcinoma and other 11 pathological subtypes (10). CCC, papillary carcinoma and chromophobe cell carcinoma are the most common types, where the proportion of clear cell carcinoma is the largest, and the degree of malignancy than papillary carcinoma and chromophobe cell carcinoma is higher with poor prognosis (11). Some patients upon physical examination were

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found with obvious symptoms of low back pain, haematuria, abdominal mass triad, but there were some patients without obvious symptoms of treatment. This significant difference in diagnosis assures a proper treatment of kidney cancer differentiating from radical nephrectomy to partial nephrectomy. Therefore, early diagnosis and accurate preoperative classification ensures an early line of proper treatment for renal cancer. All the renal cancers are treated similarly which are diagnosed at an early stage, CCC tends to be more aggressive compared to other renal cancers which generally have slower growth. Recently, American Urological Association suggests for partial nephrectomy as a standard of care for the treatment of the clinical T1 renal mass and also suggests for radical nephrectomy where partial nephrectomy is not possible. Patients who are at high surgical risks and tends to avoid the surgical procedure are kept under active surveillance and ablative techniques are applied (12). The growth rate for small renal mass less than 3 cm have low metastatic potentiality which has been found in recent studies(13-19).

We tried to indicate by this study that the imaging features of the CCC and their relationships which may help the clinician to choose an option from active surveillance, ablative technique, radical or partial nephrectomy to treat the patient accordingly. The standard procedure for diagnosis of CCC is biopsy but biopsy is an invasive technique along with sampling error(20-23). CECT and MRI are widely used standard non-invasive techniques for the diagnosis of CCC. However malignant and benign renal neoplasms can be relatively identified by using diffusion-weighted MRI(24,25).

In our article we evaluated different CT parameter of CCC and analyzed their relationship. The association of larger tumor size with higher grade, stage and metastasis has been described in previous reports of Umbreit et al, 2012, and Zhang et al, 2012(26,27). Sheir et al found that cystic degeneration is more evident in CCC(28) . In our study, we found the associations of larger tumor size with irregular shape of tumor, central necrosis of tumor, and bigger involved portions of the kidney, which means the bigger the tumor was, the more irregular in shape and necrotic the lesion was. In terms of the enhanced features, Herts et al, Ruppert Kohlmay et al, and Sheir et al have described that the degree of enhancement was most valuable parameter for the differential diagnosis of CCC from other subtypes(29,30) . However, in the present study we found more relations between the types of enhanced curves and other evaluated parameters. For instances, we described the relationship of the tumor size and enhancement curve type: the bigger tumor trends to type III while small ones trend to type I and II, which results from that the more bleeding and necrosis in large tumor can influence the blood supply and enhanced mode of the tumor. Thus, we should pay attention to the differential diagnosis between the bigger renal CCC with type III of enhanced curve and other hypo-vascular diseases, such as papillary carcinoma and chromophobe cell carcinoma. In addition, our results showed that the hyper-vascular CCCs were closely related to the lesions with type I and II of enhanced curves, which also was consistent with the mechanism. Interestingly, the study showed that the the hyper-vascular CCCs were closely related with the lesions with more necrosis and heterogeneous enhancement. In theory, hyper-vascular tumors should show homogeneous enhancement and have less necrosis because of more blood supply. We speculate the reason of this is that the tumor cells may grow quickly because of the hyper-vascularity and thus rapidly invade into or compress the blood vessels and then bring about the necrosis and homogeneous enhancement. On the other hand, we also found that the lesions with unclear rim were likely with type I and II of enhanced curves, and the possible reason maybe result from that the tumor with rapid growth rate often lacks clear boundaries. Moreover, our results showed the irregular and large lesion with a mean diameter of 10.57 cm may have more chances of rteriovenous malformation, which indicates the large mass usually requires more blood supply, and thus a large number of messy surrounding collateral vessels may promote the formation of arteriovenous malformation. In the present study, we found the metastasis was closely related to the CCC with heterogeneous enhancement and necrosis. Most of heterogeneous and necrotic CCCs in the study are large in size, and the necrosis in the tumor also indicates the tumor cell has more rapid growth than angiogenesis, which means more metastasis.

We found few potential limitations while conducting this study. First, the study was retrospective study resulting in loss of patients follow up. Second, we did the study only on CCC excluding any other renal carcinoma types. Third, the study was carried out in only one hospital resulting in coverage of limited amount of population, single race, and same area. Fourth, due to limitation of time the sample size was very less.

In conclusion, renal clear cell carcinoma has certain CT impact characteristics. Multislice spiral CT can clearly show many important manifestations of the tumor such as the necrosis, arteriovenous malformations, enhanced patterns, degrees and curves, which may reflect more biological behaviors of renal CCC, and provide more detailed information for the differential diagnosis and further treatment.

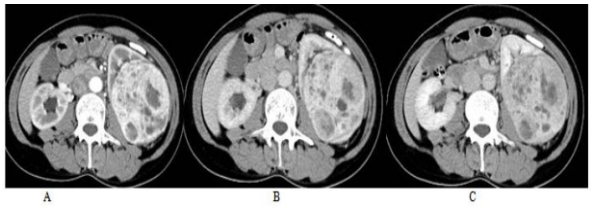

Fig 1: A 49-yr female patient. Triphasic CT shows a large CCC in the left kidney with marked and heterogeneous enhancement and clear rim and necrosis .

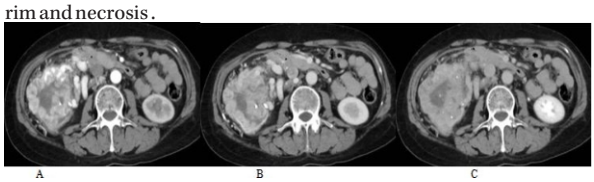

Fig 2: A 51-yr female patient. The Triphasic CT shows a large CCC in the right kidney with marked and heterogeneous enhancement, central necrosis classifications and unclear rim. Notice so many tortuous collateral vessels around the mass.

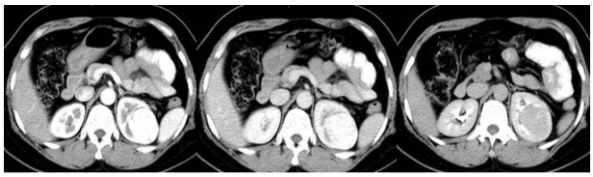

Fig 3: A 57-yr male patient. Triphasic shows a CCC in the left kidney with marked and homogeneous enhancement and clear rim.

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