## ORIGINAL ARTICLE

## Analysis of CT, MRI imaging features of renal cell carcinoma with different histopathological types

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## Summary

**Purpose:** This study aimed to investigate the computed tomography (CT) and magnetic resonance imaging (MRI) features of different histological types of renal cell carcinoma (RCC) (clear cell RCC (ccRCC), papillary RCC (pRCC), chromophobe RCC (chRCC).

**Methods:** The clinical data of 67 patients (including 38 patients with ccRCC, 20 patients with pRCC and 9 patients with chRCC) with RCC confirmed pathologically in the Affiliated Hospital of Jining Medical University were retrospectively analyzed. All patients underwent CT, MRI plain scan and three-phase enhanced scan, and their CT and MRI imaging features were analyzed.

**Results:** Most of the enhancement was non-uniform. Most of the lesions presented as "fast-in, fast-out", with obvious enhancement in the early stage and enhancement decline in the later stage. Non-uniform and slightly higher signals were mostly present in DWI. The CT scan of pRCC patients showed equal density and homogeneous enhancement. Some of the larger lesions showed cystic necrosis and hemorrhage. MRI showed a lower signal on T1WI and a slightly higher signal on T2WI. The CT of patients with chRCC showed equal density and more uniform enhancement. DWI showed high signal, and central radial scar showed low signal. There was a significant difference in the percentage of cystic necrosis in ccRCC, pRCC and chRCC among groups (p<0.05). The incidence of cystic necrosis in ccRCC and pRCC was significantly higher than that in chRCC (p<0.05). The CT values in ccRCC patients were significantly higher than those in pRCC and chRCC patients in the parenchymal phase, corticomedullary phase and excretory phase (p<0.05). The CT value of chRCC patients in the parenchymal phase was significantly higher than that of pRCC (p<0.05

**Conclusion:** The CT and MRI of ccRCC, pRCC and chRCC have their own imaging characteristics, which has important reference value for the preoperative differential diagnosis of RCC.

*Key words:* clear cell renal cell carcinoma, papillary renal cell carcinoma, chromophobe renal cell carcinoma, CT, MRI.

## Introduction

Renal cancer is the most common malignant tumor of the kidney, accounting for about 3-5% of all malignant tumors in adult men and women. The disease is the seventh most common cancer in men and the 10th most common cancer in women. Renal cell carcinoma (RCC) accounts for about 80% of kidney cancers [1]. Over the past two decades, the subtype of RCC were reclassified as its histopatho-

logical and molecular characteristics progressed. The main subtypes with an incidence > 5% were clear cell carcinoma (cRCC), papillary RCC (RCC) and chromophobe RCC (chRCC), of which ccRCC is the most common subtype and the main cause of death in patients with renal cancer [2]. pRCC, which accounts for about 15% of kidney cancers, is a heterogeneous disease consisting of multiple types of

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renal carcinoma cells, including inert, multifocal or invasive, and highly lethal phenotypes single tumors [3]. chRCC, which accounts for only about 5% of RCC, is a kidney cancer subtype with good prognosis. It usually shows relatively inert local growth pattern, but it may also be aggressive and show resistance to treatment when metastasis worsens [4].

In all renal tumors, ccRCC cells are very discrete and more prone to distant metastasis, so ccRCC is more aggressive and requires more aggressive therapeutic strategies in clinical practice, such as complete nephrectomy. pRCC,chRCC and benign tumors can be treated conservatively in specific cases [5,6]. Previous studies have shown that the 5-year overall survival time of ccRCC,pRCC and chRCC is not the same, and the survival time of the latter is significantly better than that of the former two [7]. Confirming the histological type of the RCC before the operation is of great significance for the selection of the clinical treatment plan and the evaluation of the prognosis of the RCC.

With the development of medical imaging technology, CT and MRI have been widely used in the diagnosis of renal occupying lesions and played an important role in the diagnosis of RCC [8]. However, most of the histological types of RCC are confirmed by pathology after operation, creating a certain trauma [9].

The purpose of this study was to identify the histologic types of RCC before operation by comparing CT and MRI features of the patients with ccRCC, pRCC and chRCC to provide a reference for the choice of treatment and prognosis of RCC.

## Methods

#### General materials

The clinical data of 67 patients with pathologically confirmed RCC were retrospectively analyzed. There were 38 ccRCC patients (24 males and 14 females), aged 42-79 years (mean 53.7  $\pm$ 8.9) and mean duration of disease 1.8  $\pm$ 0.9 years. There were 20 pRCC patients (12 males and 8 females) aged 39-81 years: (mean 55.8  $\pm$ 8.1) and mean duration of disease 1.7  $\pm$ 0.8 years. There were 9 chRCC patients (5 males and 4 females) aged 40-82 years (mean 54.2  $\pm$ 9.1) years; the average duration of disease was 2. 1  $\pm$ 1.3 years.

#### Inclusion and exclusion criteria

*Inclusion criteria:* histological type pathologically confirmed after the operation [10]. The subjects and families of the study have been fully informed and provided signed informed consent.

#### Exclusion criteria

Serious artifact in the lesion area; the patients had cardiac pacemaker, patients with severe heart, liver and kidney dysfunction, hematopoiesis dysfunction, other tumors, systemic autoimmune diseases, connective tissue diseases, infectious diseases, history of iodine intake, family history of mental illness and psychosis and confusion.

This study has been approved by the Ethics Committee of the affiliated hospital of Jining Medical University.

#### Computed tomography (CT)

The patients were examined by Siemens Sensation 64-row spiral CT scanner (Siemens Medical Systems, Erlangen, Germany). After iodine allergy test, and fasting for 8 h before examination, 90 mL of water-soluble iodine-containing contrast agent was injected into the anterior elbow vein at a speed of 2 to 3 mL/s, and then scan followed. Scan condition: layer thickness interval 3.2 mm or 6.5 mm; pitch 0.5. From the superior margin of the liver to the anterior superior iliac spine, the parenchymal phase, the corticomedullary phase and the excretory phase were enhanced and the breath-holding time was 20-30 s. The images were transmitted to the workstation for observation, measurement, reconstruction and statistics. The CT value and length of the lesion were measured, and the enhancement intensity, enhancement pattern, cystic change, calcification and necrosis of the lesion were evaluated. The scanned images were evaluated and analyzed by two experienced radiologists in the Affiliated Hospital of Jining Medical University.

#### Magnetic resonance imaging (MRI)

Siemens 1.5T MRI (Siemens Medical Systems, Erlangen, Germany) was used to examine the patients (fasting for 8 h before examination). The patient was in supine position and the long axis of the body was consistent with that of the bed. Transverse and coronal position used T1WI and T2WI plain scan. Transverse: matrix was 256 ×160-224, interval was 1.2 mm, layer thickness was 6 mm, TR/TE parameter was 1000ms/91 ms. Coronal position: matrix was 256 ×256, interval was 1.5mm, layer thickness was 5mm, TR/TE parameter was 4.3ms/2.15 ms. 10-20 ml of contrast agent (Shandong Jinan Hongfangde Pharmaceutical Technology Co., Ltd., China, No. 0003) was injected into the anterior elbow vein and then enhanced scanning was performed. The delay time of the parenchymal phase, corticomedullary phase and excretory phase were 23 s, 70 s and 60-70 s, respectively. The signal intensity (low, equal and high signal), enhancement intensity, edge of the lesion, cystic change, calcification of the lesion and envelope around the lesion were observed. The scanned images were evaluated and analyzed by two experienced radiologists in the Affiliated Hospital of Jining Medical University.

#### Statistics

SPSS23.0 (IBM Corp, Armonk, NY, USA) was used for statistical analyses. GraphPad Prism 7 was used to draw Figures of the data. Counting data were expressed by case/percentage [n (%)]. Chi-square test was used to compare the data of inter-group counting. The continuous correction chi-square test was used when the theoretical frequency was less than 5. The measurement data was expressed by mean ±standard deviation (x ±sd). T-

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test of independent samples was used to compare the measurement data between groups. One-way ANOVA was used to compare data among groups, and then SNK-q test was used to compare two groups. When p<0.05, the difference was statistically significant.

## Results

### General materials

There was no significant difference in sex, age, body mass index (BMI), course of disease, smoking history, drinking history, physical examination findings, hematuria, backache, lesion region, mean diameter of tumor, lymph node metastasis, Fuhrman grade and TNM stages of ccRCC, pRCC, chRCC patients (p>0.05) (Table 1). Characteristics of CT and MRI scanning in patients with ccRCC, pRCC and chRCC

CT plain scan showed 21 cases of equal density and 17 cases of low density in ccRCC patients. Most of the enhancement was non-uniform. Most of the lesions presented as "fast-in, fast-out", with obvious enhancement in the early phase and the enhancement declined in the later phase. MRI scan showed 30 cases of equal signal and 8 cases of low signal on T1WI, 19 cases of high signal, 17 cases of equal signal and 2 cases of mixed signal on T2WI. Non-uniform and slightly higher signals were mostly present in DWI. The CT scan of pRCC patients showed equal density and homogeneous enhancement. Some of the larger lesions

Table 1. General information of ccRCC, pRCC, chRCC patients [n (%)] / (x±sd)

Classification	ccRCC (n=38)	pRCC (n=20)	chRCC (n=9)	$F/x^2$ value	p value
Sex				0.194	0.908
Male	24 (63.16)	12 (60.00)	5 (55.56)		
Female	14 (36.84)	8 (40.00)	4 (44.44)		
Age (years)	53.7±8.9	55.8±8.1	54.2±9.1	0.385	0.682
BMI (kg/m <sup>2</sup> )	22.38±2.86	22.61±2.73	23.19±2.38	0.317	0.729
Course of disease (years)	1.8±0.9	1.7±0.8	2.1±1.3	0.577	0.565
Smoking history, n (%)				0.822	0.663
Yes	20 (52.63)	13 (65.00)	5 (55.56)		
No	18 (47.37)	7 (35.00)	4 (44.44)		
Drinking history, n (%)				0.234	0.890
Yes	22 (57.89)	12 (60.00)	6 (66.67)		
No	16 (42.11)	8 (40.00)	3 (33.33)		
Physical examination findings, n (%)				1.153	0.562
Yes	14 (36.84)	10 (50.00)	3 (33.33)		
No	24 (63.16)	10 (50.00)	6 (66.67)		
Hematuria, n (%)				1.776	0.412
Yes	15 (39.47)	5 (25.00)	2 (22.22)		
No	23 (60.53)	15 (75.00)	7 (77.78)		
Backache, n (%)				1.581	0.454
Yes	9 (23.68)	6 (30.00)	4 (44.44)		
No	29 (76.32)	14 (70.00)	5 (55.56)		
Lesion region, n (%)				1.490	0.475
Left kidney	17 (44.74)	9 (45.00)	6 (66.67)		
Right kidney	21 (55.26)	11 (55.00)	3 (33.33)		
Mean tumor diameter (cm)	6.6±3.7	6.2±2.3	6.2±2.9	0.125	0.883
Lymph node metastasis, n (%)				0.354	0.838
Yes	7 (18.42)	5 (25.00)	2 (22.22)		
No	31 (81.58)	15 (75.00)	7 (77.78)		
Fuhrman grade , n (%)				0.540	0.764
I-II	23 (60.53)	14 (70.00)	6 (66.67)		
III-IV	15 (39.47)	6 (30.00)	3 (33.33)		
pT phase, n (%)				0.782	0.676
pT1-pT2	25 (65.79)	11 (55.00)	5 (55.56)		
рТ3-рТ4	13 (34.21)	9 (45.00)	4 (44.44)		

showed cystic necrosis and hemorrhage. MRI showed a lower signal on T1WI and a slightly higher signal on T2WI. Pseudocapsule was seen in 11 cases at the late enhancement phase. The CT of patients with chRCC showed equal density and more uniform enhancement. On MRI, T1WI showed equal signal, T2WI showed 3 cases of equal signal, 6 cases of slightly low signal, 7 cases of homogeneous enhancement and 2 cases of inhomogeneous enhancement, of which 7 cases showed central strip low signal after the delay. DWI showed high signal, and central radial scar showed low signal.

## Features of common CT and MRI signs in ccRCC, pRCC, chRCC

The main features of CT and MRI in RCC patients were hemorrhage, cystic necrosis, peripheral invasion, lymph node, pseudocyst and venous tumor thrombus. The results of CT and MRI showed that there was a significant difference in the percentage of cystic necrosis in ccRCC, pRCC and chRCC among groups (p<0.05). The incidence of cystic necrosis in ccRCC and pRCC was significantly higher than in chRCC (p<0.05). There was no significant difference in the incidence of cystic necrosis between ccRCC and pRCC (p>0.05). There was no significant difference in bleeding, peripheral invasion, calcification, pseudocapsule and venous tumor thrombus in ccRCC, pRCC and chRCC (p>0.05) (Tables 2 and 3).

# CT value of enhanced scanning at different stages of cortex in patients with ccRCC, pRCC and chRCC

The CT values in ccRCC patients were significantly higher than in pRCC and chRCC in the parenchymal phase, corticomedullary phase and excretory phase (p<0.05). The CT value of chRCC patients in the parenchymal phase was significantly higher than in pRCC (p<0.05) (Table 4).

0 (0.00)

p value

0.214

< 0.001

0.351 0.482

0.324

0.241

2.843

Features of signs	ccRCC (n=38)	pRCC (n=20)	chRCC (n=9)	<b>x</b> <sup>2</sup>
	n (%)	n (%)	n (%)	
Haemorrhage	8 (21.05)	2 (10.00)	0 (0.00)	3.085
cystic necrosis	33 (86.84)*	12 (60.00)*	0 (0.00)	2.550
Peripheral invasion	5 (13.16)	1 (5.00)	0 (0.00)	2.092
Calcification	6 (15.79)	1 (5.00)	1 (11.11)	1.458
Pseudocapsule	17 (44.74)	5 (25.00)	3 (33.33)	2.253

#### Table 2. Features of CT signs in patients with ccRCC,pRCC and chRCC

venous tumor thrombus Compared with chRCC, p<0.05.

#### Table 3. Features of MRI signs in patients with ccRCC, pRCC and chRCC

6 (15.79)

Features of signs	ccRCC (n=38)	pRCC (n=20)	chRCC (n=9)	<b>x</b> <sup>2</sup>	p value
	n (%)	n (%)	n (%)		
Haemorrhage	8 (21.05)	5 (25.00)	0 (0.00)	2.633	0.268
cystic necrosis	34 (89.47)*	15 (75.00)*	0 (0.00)	29.700	< 0.001
Peripheral invasion	5 (13.16)	2 (10.00)	1 (11.11)	0.131	0.967
Calcification	7 (18.42)	2 (10.00)	1 (11.11)	0.851	0.654
Pseudocapsule	19 (50.00)	11 (55.00)	4 (44.44)	0.296	0.862
Venous tumor thrombus	7 (18.42)	1 (5.00)	0 (0.00)	3.654	0.161
* 1 11 1 2 2 2 2 2					

1 (5.00)

\*compared with chRCC, p<0.05.

#### Table 4. CT value of enhanced scanning at different stages of cortex in patients with ccRCC, pRCC and chRCC

Features of signs	ccRCC (n=38)	pRCC (n=20)	chRCC (n=9)	F value	p value
Parenchymal phase	95.18±24.35* <sup>,#</sup>	75.34±8.25	81.22±12.63*	7.250	0.002
Corticomedullary phase	118.59±14.37 <sup>&amp;</sup>	66.42±12.89	65.37±11.75	121.900	< 0.001
Excretory phase	72.48±16.53 <sup>&amp;</sup>	61.57±9.58	60.41±4.26	5.594	0.006

\*compared with pRCC, p<0.05; \*compared with chRCC, p<0.05; &compared with pRCC and chRCC p<0.05.

## Discussion

RCC is an epithelial tumor derived from the proximal tubules of the renal unit, of which ccRCC, pRCC, chRCC are the most common subtypes [11,12]. Imaging is the most important diagnostic method of RCC. In particular, the rapid development of CT and MRI techniques greatly improved the diagnostic value of renal lesions in clinical practice and provide a certain basis for the early diagnosis of RCC [13,14]. However, there are some differences in the selection of RCC treatment of different subtypes [15], so it is very important to distinguish the different types of RCC in the early stage of disease.

ccRCC is derived from the proximal tubule epithelial cells, and the main growth mode is expansibility, and most of them are solitary. Macroscopically, it is a kind of substantial yellow lesion with uneven texture with varying degrees of internal necrosis, cystic degeneration, hemorrhage and calcification, and some with pseudocapsular growth [16]. In this study, the MRI for ccRCC patients showed an equal and low signal on T1WI and equal, high and hybrid signal on T2WI. Most of DWI were non-uniform, with slightly high signal, and MRI was nonuniform. CT showed equal and low density. Most of the enhancement was non-uniform. Most of the lesions presented as "fast-in, fast-out", with obvious enhancement in the early stage and enhancement decline in the later stage with hemorrhage, cystic necrosis and pseudocyst. This is similar to the study of Mo et al [17] where CT scan of ccRCC patients showed equal and low density and "fast-in, fast-out" characteristics. In the research of Yu et al [18], lesions with ccRCC metastasis to the pancreas showed single or multiple nodules or masses with slightly low or equal density and blurred boundaries on unenhanced CT; the enhancement pattern of pancreatic lesions was similar to that of ccRCC and showed "fast-in, fast-out" features on enhanced CT. It may be that ccRCC is a tumor with rich blood supply, and there is a thin vascular network in the lesion [19], so the enhancement of CT and MRI is mostly non-uniform. pRCC is the second most common subtype of RCC and is a solid tumor. CT was not enhanced significantly [20]. In this study, the CT scan of patients with pRCC showed iso-density lesions, and some of the larger lesions showed cystic necrosis and hemorrhage. MRI showed a slightly low signal on T1WI and a slightly high signal on T2WI, and the late enhancement showed pseudocapsule. In the study of Herts et al [21], pRCC usually had few blood vessels and was homogeneous. If the enhancement of tumor parenchyma is more than 25%, it basically excludes the possibility of pRCC.

It may be that most of pRCC lack blood supply [22], so the corticomedullary phase mostly shows moderate enhancement, and the intensity of enhancement is lower than that of ccRCC. ChRCC is a rare subtype of RCC with the best prognosis in RCCs. Most patients with chRCC have no typical clinical manifestations (mass, backache and hematuria) [23,24]. chRCC cystic lesions and necrosis are rare, like perirenal infiltration and vascular involvement, the main features of which are enhancement of central stellate scar and spoke [25]. In this study, the CT of patients with chRCC showed equal density, and MRI mostly showed equal signal on T1WI, equal and slightly lower signal on T2WI. Enhanced CT and MRI showed uniform enhancement, and DWI showed high signal. After the delay, the central strip-like low signal could be seen, which had been reported as "spoke-wheel sign" [26]. This is similar to the performance of chRCC (chRCC shows relatively uniform enhancement and has a typical spoke pattern) in CT and MRI reported by Prasad et al [27]. In the study of Sun et al [28], the cortical intensity enhancement index of ccRCC was the highest on the images of cortical medulla and nephrographic phase, and the signal intensity of ccRCC was significantly higher than that of pRCC. The enhancement index of pRCC was the smallest and chRCC was in the middle. In the research of Young et al [29], the signal intensity of ccRCC in the cortical phase was significantly higher than in oncocytoma, pRCC and chRCC. After controlling tumor size, age and sex, the relative cortical signal intensity can distinguish ccRCC from other renal cell subtypes. In this study, the CT values in ccRCC patients were significantly higher than in pRCC, while in chRCC patients in the parenchymal phase, corticomedullary phase and excretory phase, the CT value of chRCC patients in the parenchymal phase was significantly higher than in pRCC. Therefore, it may be more meaningful to synthesize the CT and MRI signal strength of ccRCC, pRCC and chRCC to identify the tissue types of RCC.

Although this study confirmed that there are some differences in the features of CT and MRI of different histologic RCCs, there are still some overlap in the characteristics of CT and MRI plain scan and enhancement. Therefore, clinical symptoms, signs and laboratory results should be closely combined to reduce the rate of misdiagnosis.

In conclusion, the CT and MRI of ccRCC,pRCC and chRCC have their own imaging characteristics, which has important reference value for the preoperative differential diagnosis of RCC.

### **Conflict of interests**

The authors declare no conflict of interests.

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