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Original Article

Multidetector Computed Tomography Evaluation of Subtypes of Renal Cell Carcinoma

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Abstract

Introduction: Renal cell carcinoma (RCC) accounts for approximately 5% of all cancers in men and 3% in women and is the second most common urologic neoplasm.[1]

Aim: The purpose of our study is to identify the different demographic characteristics of patients with RCC, to study different features of subtypes on multidetector computed tomography (MDCT), and to determine the differentiating features of subtypes.

Materials and Methods: We reviewed four subtypes of RCC. 24 patients with RCC who underwent nephrectomy, pre-operative MDCT evaluation, and with pathological diagnosis of RCC were included in our study. Features of tumors and attenuation pattern in CT were evaluated and analyzed.

Results: The clear cell RCC was the most common (75%) tumor subtype with smaller size of the lesion at presentation, heterogeneous enhancement, and cystic degeneration, hypervascularity with post-contrast HU of >100 in corticomedullary phase. The tumor had various patterns of spread and the tumor to aorta enhancement ratio was >0.3. The papillary RCC (pRCC) was 17%, smaller lesions, and hypovascular with post-contrast HU of <100. The tumor-to-aorta enhancement ratio was <0.23. Single case of translocation type RCC (4%) and chromophobe RCC (4%) were observed which presented with intermediate features and tumor-to-aorta enhancement ratio was 0.3 and 0.23-0.3, respectively. Chromophobe RCC showed calcification and high-attenuation values. Excepting pRCC, other subtypes were observed more in females.

Conclusion: In addition to CT tumor attenuation values, the combination of other parameters play an important role in diagnosing and differentiating among the different subtypes of RCC. Other important differentiating parameter observed was tumor-to-aorta enhancement ratio.

Key words: Chromophobe, Clear cell, Papillary, Subtypes

INTRODUCTION

Renal cell carcinoma (RCC) accounts for approximately 5% of all cancers in men and 3% in women and is the second most common urologic neoplasm.[1] RCC accounts for 85-90% of all kidney tumors, representing 1-3% of all malignant visceral neoplasms and have maintained an increasing prevalence.[1,2] Clear cell RCC is the most common variety accounting for 70% followed by papillary RCC (pRCC) 10%, chromophobe RCC (Chr RCC) 5%, collecting duct carcinoma - <1%, medullary carcinoma <1%, mucinous tubular and spindle cell carcinoma - <1%, neuroblastoma-associated RCC - <1%, Xp 11.2 translocation - TFE3 carcinoma - <1%, and unclassified lesions - 4%.[2]

Early mortality of most of the (40%) of patients with RCC is because of the disease progression, advanced stage at presentation, and delayed diagnosis. Thus, this tumor is the most lethal malignant urological tumor. The histological classification of RCCs is extremely important, due to implications of the subtypes in the prognosis and treatment of these tumors.[3,4] In this context, a pre-operative radiological characterization of RCCs subtypes is of utmost importance and depending on the clinical situation, it may be supplemented or not by confirmatory percutaneous biopsy.[5,6]

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In 2013, the International Society of Urological Pathology proposed a new RCC classification including the WHO proposal but suggesting the inclusion of five new, well-characterized types of renal neoplasm, and three additional types considered as new and emerging entities.[7]

Imaging methods play a relevant role in the diagnosis of RCCs, determining a tendency toward the diagnosis of tumors at earlier stages, besides being essential for staging and therapeutic planning.[8] Most of the renal tumors are discovered on imaging studies for urological or other concerns. And also, some past studies proved the possibility of histological diagnosis of renal tumors by imaging features. Computed tomography (CT) has been widely used for the evaluation of RCC because it can provide detailed information about the tumor itself and its perinephric extension, extension to renal vein and lymphatic spread. Furthermore, with the use of helical CT, it is possible to analyze the enhancement pattern of the tumor. All the previous studies reported that stronger enhancement pattern was the most important differentiating feature among the subtypes. In addition, the study conducted by Herts *et al*. discussed another parameter of tumor-to-aorta enhancement ratio, which when considered the sensitivity of diagnosing papillary cell carcinoma increases by 50%.[9]

Aim

The current study was aimed to study the demographic characteristics and main imaging findings of the histological RCC variants in author's current location on multidetector CT (MDCT) and to study the important imaging features to differentiate among the subtypes.

MATERIALS AND METHODS

Patients

This is a retrospective study. We used our institutional database to identify patients who underwent surgical management of renal tumors from January 2011 to May 2015. This study was conducted after obtaining the approval from the Institutional Review Board to review the patients images and medical charts. Patients who had pre-operative CT evaluation in our institution according to our institution's renal mass protocol involving four phases (unenhanced, corticomedullary, nephrographic, and excretory) and had confirmed the pathological diagnosis of subtype of RCC were included in this study. The study population included were 24 patients.

CT Examination

All the MDCT examinations were performed using 16-slice GE Lightspeed CT scanner. Unenhanced and contrast material enhanced CT scans were performed in suspended inspiration. Intravenous contrast was given as Omnipaque 300 (Iohexol) 150 ml bolus containing 40-45 g of iodine through antecubital vein at a rate of 2-4 ml/s. Scanning parameters were: Collimation - 1.3 mm, pitch - 2:1, subsecond scan time, kVp - 120, and mAs - 210. Images were obtained with unenhanced scan (negative oral contrast, Mannitol), post-contrast scan - the corticomedullary phase with scan delay of 25-70 s, nephrographic phase with scan delay of 80-180 s, and the excretory phase with scan delay of approximately 180 s were done.

Imaging Evaluation

Two radiologists independently reviewed the contrast-enhanced computed tomography (CECT) images in consensus. The following parameters were studied.

1. The demographic features of the patients underwent study
2. Imaging features of the renal tumors on plain and CECT in four phases were evaluated. Lesion size, presence, type and attenuation, calcification and characteristics of tumor spread, and metastases. The attenuation values were obtained in all four phases using ROI of 1-3 cm^2. Average of three readings was taken along the circumference of the tumor. Attenuation values were obtained separately for cortex and solid-enhancing area of the tumor.

Data Analysis

The data were analyzed using SPSS program. The results were presented using tables.

RESULTS

CT images of 24 patients were retrospectively reviewed by two radiologists. The incidence of RCC was more in the patients in 40-59 age group (83%). The male-to-female ratio observed was 11:13 and side of the kidney involved showed no difference (Table 1).

Four subtypes of RCCs were observed in our study and were cRCC (Figure 1), pRCC (Figure 2), Xp 11.2 translocation-TFE3 carcinoma (translocation RCC, TrRCC) (Figure 3), and Chr RCC (Figure 4). Most common subtype observed was clear cell carcinoma, followed by pRCC. One case of translocation RCC and one case of Chr RCC were observed (Figure 5).

Characteristics of Clear Cell Renal Cell Carcinoma (Figure 1)

Demographic characteristics

According to our study, cRCC was more common among females (56%) in 40-59 years (89%) age group and was predominantly in the right kidney (61%) (Table 2).

Characteristics of lesion

Most of the tumors (56%) were smaller (≤200 cc) at presentation with smooth margins (89%), heterogeneous enhancement pattern and with cystic degeneration (89%). Very few (11%) presented with calcifications (Table 3). The tumor-to-aorta enhancement ratio observed was >0.3. The attenuation of solid areas of tumor on CECT was high and was paralleling the renal cortex (75-145 HU) than the papillary, chromophobe, and translocation types which were comparatively low in attenuation (Table 4).

Spread of the disease

The cRCC spread was mainly to the perinephric fat (67%). Local spread to the adjacent organs was less (11%). Other way of spread observed was through the ureter (11%), renal vein (33%), and inferior vena cava (IVC) (22%). Lymphatic spread to regional lymph nodes was more (78%). In our study, no distal lymph node involvement was observed. The metastatic spread was less (11%) and was mostly (60%) to the lung followed by to liver and bones (lumbar vertebrae) (Tables 5 and 6).

Papillary Renal Cell Carcinoma (Figure 2)

The age distribution of pRCC was similar to clear cell carcinoma (44-48 years), and the male-to-female ratio was 3:1. Our study showed more predilection of pRCC to left kidney (Table 2). The size of the lesion at presentation was smaller compared to cRCC (32-90 cc) with no calcifications observed within the lesion

Table 1: Distribution of demographic characteristics of the patients with RCC

Characteristics	*N*=24 (%)
Age range (years)	
<10	1 (4.1)
10-39	1 (4.1)
40-49	14 (58.3)
50-59	6 (25)
60-69	2 (8.33)
Distribution of the patients according to sex	
Male	11 (45.8)
Female	13 (54.2)
Side of the kidney involved	
Right	12 (50)
Left	12 (50)

RCC: Renal cell carcinoma

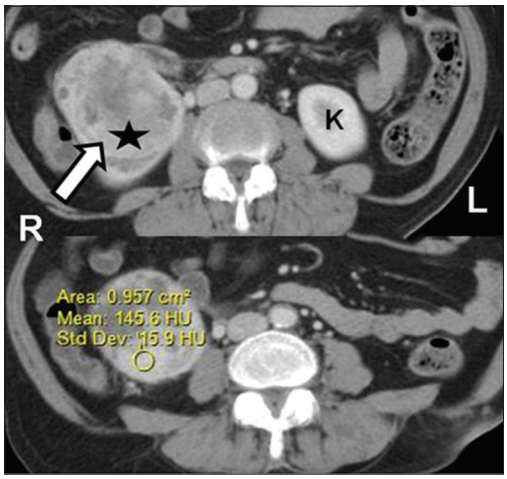

Figure 1: Clear cell RCC: CECT - axial section of abdomen shows heterogenously enhancing mass in the right kidney with perinephric tumor spread

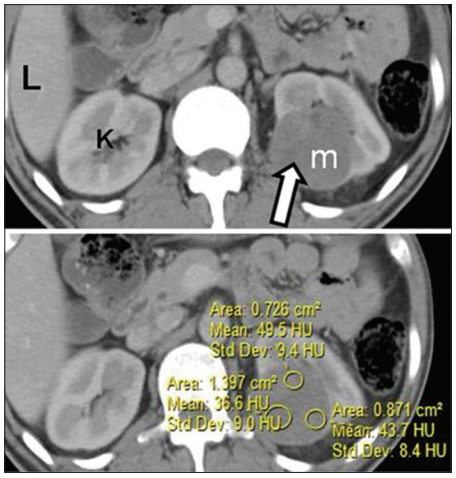

Figure 2: Papillary renal RCC: CECT axial section of abdomen shows mildly enhancing left kidney mass lesion

Table 2: Distribution of patients with RCC according to demographic characteristics and side of the kidney involved

Characteristic	Clear cell RCC *N*=18 (75%)	pRCC *N*=4 (17%)	Translocation type RCC *N*=1 (4%)	Chr type RCC *N*=1 (4%)
Age (years)				
<10	0	0	1 (7 years)	0
10-39	0	0	0	1 (27 years)
40-49	10 (55.6)	4 (100)	0	0
50-59	6 (33.3)	0	0	0
60-69	2 (11.1)	0	0	0
Sex				
Male	8 (44)	3 (75)	Nil	0
Female	10 (56)	1 (25)	1 (100)	1 (100)
Side of the kidney involved				
Right kidney	11 (61)	Nil	Nil	1 (100)
Left kidney	7 (39)	4 (100)	1 (100)	Nil

RCC: Renal cell carcinoma, pRCC: Papillary renal cell carcinoma, Chr RCC: Chromophobe renal cell carcinoma

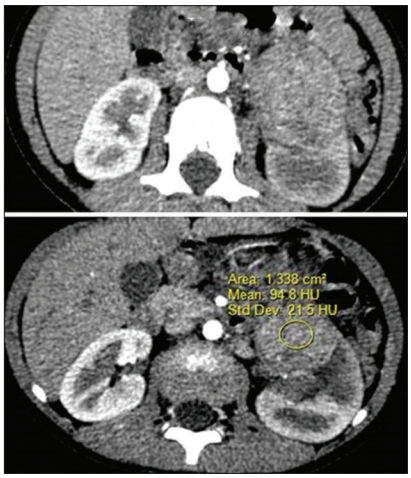

Figure 3: Translocation RCC: Well marginated, homogenously enhancing Mass lesion in the left kidney . No calcifications within.(m-mass, k-kidney, L-liver)

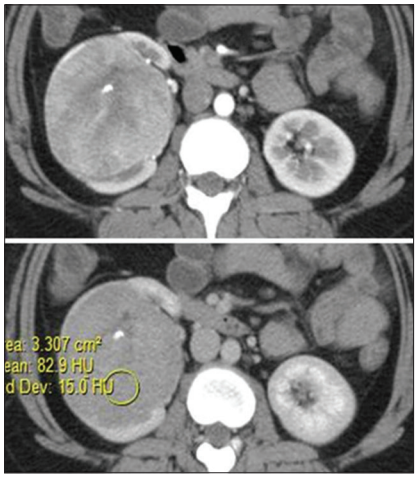

Figure 4: Chromophobe RCC: A well-defined lobulated mass lesion in the right kidney with homogenous enhancement, calcification within

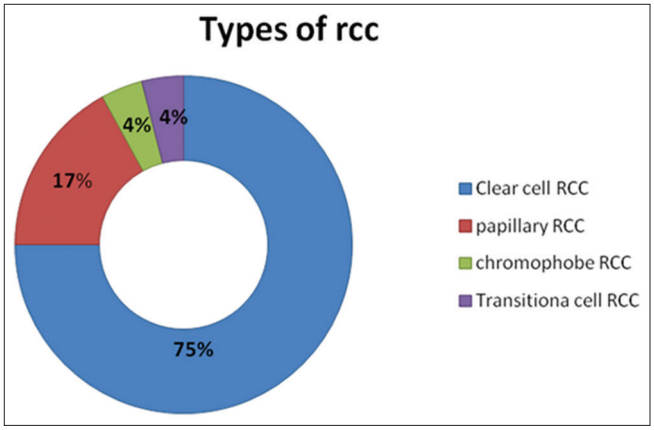

Figure 5: Types of renal cell carcinoma

(Table 3). Maximum attenuation on NECT was 43 HU and on CECT was 60 HU in corticomedullary phase with majority showed homogenous enhancement pattern. The tumor/aorta enhancement ratio was <0.3 (0.15-0.23) (Table 4). All the observed lesions showed perinephric spread. No spread was observed to the adjacent organs, renal vein, and ureter. Spread to the regional lymph nodes was 50% and no spread to the distal lymphnodes. In our study, pRCC had not showed any distal organ metastases (Tables 5 and 6).

Translocation Renal Cell Carcinoma (Figure 3)

One translocation RCC was observed in our study in female patient in pediatric age group involving the left kidney (Table 2). The size of the tumor at presentation was 40 cc, which showed regular margin with no calcification and degeneration (Table 3). The other characteristics observed were homogenous enhancement pattern. The attenuation of the mass was high compared to pRCC in NECT and CECT and low compared to cRCC. The tumor-to-aorta enhancement ratio was 0.3 (Table 4). The type of spread observed was to the regional lymphnodes. No other type of spread was observed (Tables 5 and 6).

Chromophobe Renal Cell Carcinoma (Figure 4)

A case of 27-year-old female was presented in our study (Table 2). The size of the lesion was larger (>200 cc) at presentation. The lesion is homogenous, isodense with renal parenchyma showed lobulated margin with calcifications within. No degeneration was noticed (Table 3). Post-contrast HU of the lesion was <100 and is histologically hypovascular. The tumor showed maximum enhancement in nephrographic phase compared to other subtypes. Tumor-to-aorta enhancement ratio was >0.23 and <0.3 (Table 4). No characteristic tumor spread was identified (Tables 5 and 6).

DISCUSSION

The classification of RCC was mainly based on the microscopic appearance of the tumor and genetic abnormalities. Each subtype is associated with a different prognosis and tumor behavior.[10] Patients diagnosed with papillary carcinoma and chromophobe subtype have higher 5-year survival rate than those with conventional RCC.[10,11]

There are different studies conducted for the identification of CT features of subtypes of RCC. According to them, strong enhancement equal to the renal cortex was observed in conventional RCC.[12]

In our study, we found enhancement pattern was different among four subtypes of RCC with high-attenuation values of cRCC in corticomedullary phase. The clear cell carcinoma showed strong enhancement pattern with high-attenuation values in all phases compared to other

Table 3: Distribution of patients with RCC according to tumor characteristics

Characteristic	Clear cell RCC *N*=18 (75%)	pRCC *N*=4, (17%)	Translocation RCC *N*=1 (4%)	Chr RCC *N*-1 (4%)
Size (%)				
≤200 cc	10 (55.6)	4 (32-90 cc)	1 (40 cc)	0
>200 cc	8 (44.4)	0	0	1 (100)
Margin (%)				
Smooth	16 (88.9)	2 (50)	1 (100)	1 (lobulated)
Irregular	2 (11.1)	2 (50)	0	
Calcification				
Present	2 (11.1)	0	0	1 (100)
Not present	16 (88.9)	4 (100)	1 (100)	0
Cystic degeneration				
Present	16 (88.9)	2 (50)	0	0
Absent	2 (11.1)	2 (50)	1 (100)	1 (100)

RCC: Renal cell carcinoma, pRCC: Papillary renal cell carcinoma, Chr RCC: Chromophobe renal cell carcinoma

Table 4: Distribution of patients with RCC according to CECT characteristics of tumor

Characteristic	Clear cell RCC *N*=18 (75%)	pRCC *N*=4, (17%)	Translocation RCC *N*=1 (4%)	Chr RCC *N*=1 (4%)
Enhancement pattern (%)				
Homogeneous	10 (55.6)	3 (60)	1 (100)	1 (100)
Heterogeneous	8 (44.4)	1 (40)	0	0
Tumor/aorta enhancement ratio				
<0.3		4 (0.15-0.23) (100)		1 (>0.23-0.3) (100)
0.3			1 (100)	
>0.3	18 (100)			
CECT attenuation of solid area				
Corticomedullary phase	75-145 HU	40-66 HU	94 HU	90 HU

RCC: Renal cell carcinoma, pRCC: Papillary renal cell carcinoma, Chr RCC: Chromophobe renal cell carcinoma, CECT: Contrast-enhanced computed tomography

Table 5: Distribution of patients with RCC according to characteristics of tumor spread

Characteristic	Clear cell RCC *N*=18 (75%)	pRCC *N*=4 (17%)	Translocation RCC *N*=1 (4%)	Chr RCC *N*=1 (4%)
Perinephricspread (%)				
Present	12 (67)	4 (100)	0	0
Not present	6 (33)	0	1	1
Adjacent organs				
Involved	2 (11)	0	0	0
Not involved	16 (89)	4 (100)	1	1
Ureter				
Involved	2 (11)	0	0	0
Not involved	16 (89)	4 (100)	1	1
Renal vein				
Involved	6 (33.3)	0	0	0
Not involved	12 (66.7)	4 (100)	1	1
IVC involved	4 (22)	0	0	0
IVC not involved	14 (78)	4 (100)	1	1

RCC: Renal cell carcinoma, pRCC: Papillary renal cell carcinoma, Chr RCC: Chromophobe renal cell carcinoma, IVC: Inferior vena cava

Table 6: Distribution of patients with RCC according to spread to lymphnodes and distant metastases

Characteristics	Clear cell RCC *N*=18 (75%)	pRCC *N*=4 (17%)	Translocation RCC *N*=1 (4%)	Chr RCC *N*=1 (4%)
Lymphadenopathy (%)				
Regional	14 (78)	2 (50)	1	0
Distal	0	2 (50)	0	0
Metastases				
Present	2 (11)	0	0	0
Not present	16 (89)	4	1	1

RCC: Renal cell carcinoma, pRCC: Papillary renal cell carcinoma, Chr RCC: Chromophobe renal cell carcinoma

tumors (Table 4). Similar enhancement pattern was also observed in other studies.[12,13] The strong enhancement pattern of cRCC is caused by its rich vascular network and alveolar architecture at histological examination.[10,12] In addition to enhancement pattern, calcifications, and cystic degeneration are other important differentiating features observed which in combination will help in diagnosing cRCC from other subtypes. The hemorrhage and necrosis within the tumor at pathologic examination are the cause for heterogeneous enhancement pattern.[10,14] Other important finding observed was tumor-to-aorta enhancement ratio which was >0.3 in cRCC. Spread of the lesion is another important feature which the cRCC in our study showed in addition to perinephric space spread, spread to regional lymphnodes, adjacent organs and to renal vein, IVC, ureter, and distant organ metastases.

The papillary carcinoma was the second highest incidence (17%) in our study.[15] The homogeneous enhancement pattern with less attenuation values compared to cRCC is because of hypovascularity of the tumor.[9,16,17] Calcifications were not present in our study, which was against to other studies.[16] This could be due to less number of cases. The tumor aorta enhancement ratio was <0.3 (0.15-0.23),[18] this could be again due to hypovascularity of the lesion.

Series of the previous reports on subtypes of RCC were done but less information was published regarding the XP translocation RCC, because of rarity of the tumor (<1%). Our study found one translocation RCC in pediatric age group, in female patient as described in the previous study.[19,20] The attenuation pattern of the lesion was homogenous with higher values than papillary carcinoma (58 and 90 HU), and this could be attributed to hypervascularity of the tumor. The tumor aorta enhancement ratio was 0.3. Histologically, the tumor shows hemorrhage and necrosis.[15]

A case of chromophobe RCC presented in our study showed similar features like the study conducted by Raman *et al.*[16] However, the findings cannot be compared due to single lesion.

Limitations

Main limitation of our study is smaller sample size, less number of pRCC, Chr RCC, and translocation RCC subtypes to analyze characteristic CT features. This could also be due to lower incidence of the these subtypes. However, further investigation with adequate number of sample will be necessary to study these low-incidence RCC subtypes.

CONCLUSIONS

This study indicates not only the tumor attenuation which is identified as the most important differentiating feature but also the MDCT assessed other parameters such as size at presentation, heterogeneity, tumor spread, and tumor/aorta enhancement ratio when used in combination can help to distinguish between different subtypes of RCC (especially cRCC and other RCC subtypes). Our data should be confirmed and validated by larger and prospective study.

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