

## Role of Computed Tomography in the Pre operative Diagnosis of Clear Cell Renal Carcinoma

Kaleem Ur Rahman, Ameet Jesrani\* and Mubarak Ali

Department of Radiology, Sindh Institute of Urology and Transplantation, Karachi, Pakistan

\*Corresponding author: Dr. Ameet Jesrani, Department of Radiology, Sindh Institute of Urology and Transplantation, Karachi, Pakistan, Tel: 03342629397, 03002727967; E-mail: ameeet.jesrani@yahoo.com

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### Abstract

**Background:** Renal cell carcinoma (RCC) accounts for 3% of all human malignant tumors. The behavior of RCC apparently depends on its subtype. CT scan can provide detailed information about the tumor itself and regarding its precise extension. The pre-histological diagnosis of clear cell renal carcinoma could be made with more precision on the basis of CT scan features and would ultimately play a major role in the prognosis and management of the disease.

**Objective:** To determine the diagnostic accuracy of computed tomography in the diagnosis of clear cell renal carcinoma taking histopathological findings as gold standard.

**Methods:** Total 100 patients had renal mass were included. All patients underwent contrast enhanced CT scan. On the basis of CT scan features a pre-surgical diagnosis of histological subtype of RCC, clear cell renal carcinoma was made. The patients were followed by nephrectomy. The diagnostic accuracy of CT scan was determined.

**Results:** The male to female ratio was 3.2:1.0. Out of total study subjects 85.0% patients turned out to be renal cell carcinomas and among these 40 (47%) were right sided and 45 (53%) were left sided. The mean size of tumor was 12.75 cm. The sensitivity, specificity, and diagnostic accuracy of CT scan were 89.0%, 72.7%, and 86.0% respectively.

**Conclusion:** The CT scan was helpful in diagnosing clear cell renal carcinoma. The most valuable parameter was the degree of enhancement of clear cell renal carcinoma with other parameters playing supplemental role.

**Keywords:** Diagnostic accuracy; Computed tomography; Clear cell renal carcinoma; Histopathology

### Introduction

Renal cell carcinoma accounts for 3% of all visceral malignant tumors and seventh most common histological type of cancer in the western world, proving a significant cause of morbidity and mortality [1,2]. This is the According to the First International Workshop on Renal Cell Carcinoma held by the World Health Organization, Renal cell carcinoma can be classified into Conventional or Clear cell renal carcinoma (Papillary renal carcinoma, Chromophobe renal carcinoma, Collecting duct renal carcinoma, Medullary renal carcinoma, and Unclassified renal carcinoma). Sarcomatoid degeneration can occur in all subtypes [3]. The behavior of renal cell carcinoma apparently depends on its subtype with some subtypes having comparatively favorable prognosis while others having grave. Therefore, precise prediction of the subtype preoperatively has significant implications in planning appropriate treatment options and estimating the prognosis of patients [4,5].

The five year survival rate is different amongst the various subtypes of renal cell carcinoma, for example, for clear cell it is 55-60%, papillary 80-90%, Chromophobe has the best approximately 90%, collecting duct 5%, while poorest for Medullary carcinoma with an

average survival of 15 weeks ,therefore different subtypes of renal cell carcinoma have different prognostic value [6]. Image guided biopsy provides relatively high accuracy (70-90%) in preoperative characterization of renal mass [7,8]. However, it is minimally invasive, involves risk and has limitations.

CT scan has been widely used for the evaluation of renal cell carcinoma because it can provide detailed information about the tumor itself and also regarding its precise extension [6,9,10]. The sensitivity and specificity of helical CT scan for diagnosing renal cell carcinoma is 96% and 95% respectively [11]. Contrast-enhanced helical CT scan findings like hypervascularity, calcification, pattern of enhancement etc. are variable amongst the subtypes and hence on this basis, it may help in predicting a specific histological subtype [6,12]. Amongst all these, the parameter of degree of enhancement taken in Hounsfield units (HU) in the corticomedullary and pyelographic phase has a high sensitivity of 74-84% and specificity ranging from 91-100% in differentiating clear cell from nonclear cell renal cell carcinoma [9]. Therefore the pre-histological diagnosis of clear cell renal carcinoma could be made with more precision on the basis of CT features and would ultimately play a major role in the prognosis and management of the disease.

## Materials and Methods

Total 100 patients of both gender, had renal masses diagnosed on ultrasound with age between 28 to 82 years were included in the study after taking inform concern and approval from institutional ethical committee. The study was conducted from 1<sup>st</sup> May 2010 to 31<sup>st</sup> October 2010 at department of radiology, Sindh institute of urology and transplantation, Karachi.

All CT scan were performed using GE advantage scanner (GE electrical medical systems Milwaukee, USA). All the subjects came for CT scan were called with 4 h of fasting. Venous access was obtained in the preparation room using an 18-20 G intracath in the antecubital vein or a large vein in the forearm. The subjects were trained to hold their breath with special attention to avoid the diaphragmatic motion. Frontal scout was taken, and then an unenhanced helical CT scan was performed using 7.5 mm slice thickness, pitch of 120 Kv, 100-150 mA, 0.8 s scan time and imaging reconstruction at 2.5 mm intervals from the diaphragm to mid pelvis during a single breath hold. The delay between the initiation of the injection and the scan was calculated using the "Smart Prep" option (GE medical systems). It ranged from 10 s to 25 s. Non ionic contrast (Iohexol 100-120 ml 300 mg iodine/ml) was injected at the rate of 4 ml/s with a power injector and images were taken in the corticomedullary and pyelographic phases along with coronal and sagittal reformations with same parameters. 500-22 cm, 1000 ml of oral contrast in form of water will also be given. CT scan image interpretation was performed on Advantage workstation. A specific solid part of the renal tumor was selected and the CT attenuation value of this part of the tumor was then taken in unenhanced, corticomedullary and pyelographic phases. The degree of enhancement was then calculated by taking the difference between the attenuation values in the unenhanced, corticomedullary and

pyelographic phases. Primarily on this and other CT parameters a pre-surgical diagnosis of clear cell renal carcinoma was then made. Subsequently majority of the patients underwent surgical nephrectomies for their tumors and the histological diagnosis was then compared with the CT diagnosis.

Data were compiled and analyzed using SPSS version 21. Frequency and percentages were obtained for qualitative variables and Mean  $\pm$  SD were calculated for quantitative variables. The diagnostic accuracy of CT scan was calculated by as considering histopathology as gold standard.

## Results

Mean age  $55.2 \pm 1.8$  years, ranged from 28-82 years. The male to female ratio was 3.2:1.0. Out of total patients, 85% turned out to be renal cell carcinomas. Of these 40 (47%) were right sided and 45 (53%) were left sided. Amongst these, 72 (84%) were clear cell carcinoma, 9 (11%) were papillary cell carcinoma, 4 (5%) were Chromophobe cell carcinoma. No collecting duct, Medullary or unclassified renal carcinoma was found. The rest of 15 (15%) renal masses which were diagnosed as RCC came out to be squamous cell carcinoma.

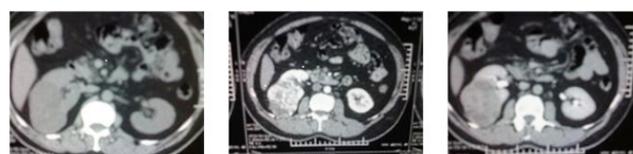
The size of tumor diameter ranged from 2.9-22.6 cm with mean tumor diameter of 12.75 cm. The tumor spread pattern of renal cell carcinoma were confined 44% to the kidney, 26% showed perinephric infiltration, 13% showed venous invasion, and 17% presented with lymphadenopathy.

Calcification was more frequently seen in papillary and Chromophobe renal carcinomas then in clear cell variant. Amongst all CT features the most important parameter was the degree of enhancement of renal cell carcinoma (Table 1).

	Unenhanced	Cortico Medullary Phase	Excretory Phase	Degree of enhancement in CM Phase	Degree of enhancement in Excretory Phase
Clear Cell RCC	26-40	89-243	63-100	63-217	37-74
Papillary RCC	32-38	53-70	42-69	21-38	10-37
Chromophobe RCC	28-48	36-59	51-56	8-31	23-28

**Table 1:** Attenuation values and degree of enhancement in HU of different Histological types of RCC.

The attenuation value of clear cell carcinoma on unenhanced CT ranged from 26-40 HU with mean of 33 HU. The attenuation values of clear carcinomas in corticomedullary phase ranged from 89-243 HU with mean attenuation value of 166 HU. The attenuation value of clear cell carcinoma in excretory phase ranged from 63-100 HU with mean of 81.5 HU. The degree of enhancement of clear cell carcinoma in the corticomedullary phase ranged from 63-217 HU with mean of 140 HU. The degree enhancement clear cell carcinoma in the excretory phase ranged from 37-74 HU with mean of 55.5 HU (Figure 1).



**Figure 1:** Clear cell carcinoma in corticomedullary and excretory phases.

The attenuation value of Chromophobe cell carcinoma on unenhanced CT was ranged from 32-38 HU with mean 35 HU. The attenuation values of Chromophobe cell carcinomas in corticomedullary phase ranged from 53-70 HU with mean attenuation value of 61.5 HU. The attenuation value of Chromophobe cell carcinoma in excretory phase ranged from 42-69 HU with mean 55.5 HU. The degree of enhancement of clear cell carcinoma in the

corticomedullary phase ranged from 21-38 HU with mean of 29.5 HU. The degree enhancement of Chromophobe cell carcinoma in the excretory phase ranged from 10-37 HU with mean of 23.5 HU (Figure 2).



**Figure 2:** Chromophobe cell carcinoma in corticomedullary and excretory phases.

The attenuation value of papillary cell carcinoma on unenhanced CT was ranged from 28-48 HU with mean 38 HU. The attenuation values of papillary cell carcinomas in corticomedullary phase ranged from 36-59 HU with mean attenuation value of 47.5 HU. The attenuation value of papillary cell carcinoma in excretory phase ranged from 51-56 HU with mean 53.5 HU. The degree of enhancement of papillary cell carcinoma in the corticomedullary phase ranged from 8-31 HU with mean of 19.5 HU. The degree enhancement of papillary cell carcinoma in the excretory phase ranged from 23-28 HU with mean of 25.5 HU (Figure 3).



**Figure 3:** Papillary cell carcinoma in corticomedullary and excretory phases.

The calculated CT scan sensitivity, specificity, PPV, NPV, and diagnostic accuracy were 89.0%, 72.7%, 92.10%, 67.0% and 86.0% in diagnosing clear cell renal carcinoma taking histopathology as gold standard.

## Discussion

The classification of renal cell carcinoma is based mainly on the histological subtypes of the tumor [1]. Each subtype is associated with a different prognosis and tumor behavior [4]. The 5 year survival rate is different amongst the various subtype of RCC, for example for clear cell it is 55-60%, papillary 80-90%, Chromophobe has the best approximately 90%, therefore different subtype of RCC have different prognostic value [13].

Precise preoperative identification of subtype of renal cell carcinoma may influence the degree of preoperative evaluation, for example metastasis survey like chest x-ray, CT scan chest and bone scanning may be avoided in a subtype that tends not metastasizes and has good prognosis and vice versa for those which have bed prognosis.

Radical nephrectomy has been indicated as a standard treatment in surgically treatable renal cell carcinoma and similarly and unnecessary wide resection may be avoided in patients with a subtype that is unlikely to recur or metastasizes. Radiation and Chemotherapy are not

usually given for the treatment of renal cell carcinoma because research shows that this type of cancer does not respond well to either therapy. However, radiation therapy may be given to people who are not candidates for surgery, or used to help alleviate pain when the cancer has spread beyond the kidneys.

Targeted therapies are designed to attack or interfere with specific genes or cells that have been shown to help with the growth of certain cancers. Drugs such as Afinitor, Sutent, Torisel, and Votrient are treatments used for advanced renal cell carcinoma, meaning the cancer has spread beyond the kidney and likely hasn't responded to other traditional treatments.

In this study, we sought to determine whether multiphase CT can help in preoperative differentiation of various types of renal cell carcinoma. Various CT parameters like size of tumor, calcification, post contrast enhancement, tumor spread and lymphadenopathy were studied. The CT findings were compared with postsurgical histopathological diagnosis which showed that out of 100 renal tumors 85 were renal cell carcinoma (RCC). Among those 85 renal cell carcinomas, there were 72 clear cell RCC, 9 papillary RCC and 4 Chromophobe RCC. The degree of enhancement was the most useful CT parameter in differentiating between subtypes of RCC.

Various CT parameters like size of tumor, pattern and degree enhancement, calcification and tumor extend that were helpful in differentiation of subtypes of RCC were studied. Amongst all these CT features the degree of enhancement was the most useful parameter in differentiating clear cell versus non-clear cell RCC. Clear cell renal carcinoma showed stronger enhancement than other subtypes of renal cell carcinomas in both the corticomedullary and excretory phases. The tumors that enhanced more than approximately 87 HU in the corticomedullary phase and 64 HU in the excretory phase were most likely to be clear cell renal carcinoma with a CT scan sensitivity and specificity of 89% and 72.7% respectively.

The results of this study are like other international studies [14-21]. The study conducted by Bird et al. [15] and Young et al. [16] also proved that RCC and Oncocytoma can be differentiated on the basis of degree on enhancement at multidetector CT. However, Zhange et al. [19] Wildberger et al. [20] and Davidson et al. [21] were unable to differentiate RCC from Oncocytoma. This was because Young et al and Bird et al has relatively larger cohort of these tumor and used four phase protocol rather than three phase protocol. In our study, no Oncocytoma was found on imaging and postoperative histopathology. The remaining 15 tumor in our study were proved to be squamous cell carcinoma.

This study has limitations like small cohort and carried out in single center. The renal masses were evaluated with standard three phase protocol. Also, we did not account for dose of contrast medium and injection rate. The strength of this study is that imaging findings were compared with histopathological diagnosis, which is the gold standard. However, our findings should be validated in larger trial in which lesions are imaged with four phase protocol.

Clear cell RCC has poorer prognosis and great likelihood of metastasis than other subtypes of RCC. In our study, overall diagnostic accuracy of CT scan was 86.0% in diagnosing clear cell renal carcinoma which is of utmost importance and depending on clinical situation; it may be supplemented or not by confirmatory image guided biopsy. It is particularly useful in clinical decision making.

## Conclusion

In conclusion, the computed tomography is helpful in diagnosing clear cell RCC and differentiating it from non-clear cell subtypes of RCC. The most valuable parameter of CT scan was the degree of enhancement of clear cell renal carcinoma with other parameters playing supplemental role.

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