Role of Multiphasic Computed Tomography in Prediction Histopathology of Renal Parenchymal Lesions

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ABSTRACT:

BACKGROUND:

Renal masses have different histologic types and subtypes, aggressiveness and metastatic potential, depending on there changes in angiogenesis

OBJECTIVE:

Is to evaluate the role of multiphasic contrast enhanced CT scan in prediction histopathology of renal masses.

PATIENTS AND METHODS:

In this prospective study, 50 patients with renal mass were diagnosed by abdominal ultrasound underwent multiphasic contrast enhanced computed tomography prior to surgical treatment,CT parameters at each phase of contrast study and histopathology results were correlated.

RESULTS:

In this study(26 female and 24 male with mean age of 55.1 ± 10.1) were evaluated, clear renal cell carcinoma was documented in 35 patients(70%), papillary renal cell carcinoma in 5 patients(10%), Wilm´s tumors in 3 patients(6%), chromophobe renal cell carcinoma in2patients(4%), angiomyolipoma in 2 patients(4%),while collecting duct renal cell carcinoma , lymphoma, and tubulocystic renal cell carcinoma were found in only one patient for each one. The correlation of mean mass density with the histopathological types revealed no statistically significant difference in noncontrast phase. Significant difference ($P<0.001$) was noted in the mean enhancement of mass between the types of RCC during corticomedullary phase, however it is insignificantly different than angiomyolipoma AML ($P>0.05$). clear cell RCC show maximum enhancement (152H.U at corticomedullary phase) with rapid wash out while papillary subtype show delayed progressive enhancement with delayed wash out with relatively low level of peak enhancement (69H.U at nephrogenic phase) AML and chromophobe RCC with other subtypes show moderately rising enhancement with presence of plateau and evidence of delayed washout. From the remaining renal masses that were hypovascular with slow pattern of enhancement during dynamic examination one in old patient proved to be lymphoma and other in pediatric age proved histologically as Wilms tumor.

CONCLUSION:

Muliphasic contrast enhanced CT is reliable modality to differentiate clear cell cancer from other subtype by maximum enhancement and rapid wash out at corticomedullary phase while papillary subtype show delay progressive enhancement with delayed wash out

KEY WORDS: multiphasic CT, Renal tumor, Renal tumor subtype.

INTRODUCTION:

Formation of new blood vessels is critical for tumor survival and growth (tumor cells release angiogenic factors that stimulate the proliferation, migration, and morphogenesis of endothelial cells), the hemodynamic characteristics of immature neovessels of tumors can be noninvasively assessed by CE-CT or CE-MRI. The principle underlying this approach is to inject a contrast agent intravenously as a bolus and measure the degree enhancement of tissue over time by using fast sequential image acquisition. The dynamics of tissue enhancement depend on:

1) The shape of the arterial input function at the entry of the tissue.
2) The kinetic distribution of the blood containing the contrast agent into the capillary bed.
3) The leakage of contrast agent across the capillary walls into the tumor interstitial (extravascular and extracellular) space, and;
4) The volume of the interstitial space where the contrast agent can diffuse [(1)].

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The CT approach is easy to implement because there is a linear relation between the attenuation numbers (expressed in Hounsfield units) and the concentration of contrast agent [2].The most commonly used method to evaluate indeterminate renal masses is contrast-enhanced CT. it is also considered the method of choice to stage renal cell carcinoma, with high accuracies in both early and advanced stages [3].

Multiphase renal CT improves the sensitivity of renal lesions detection (sensitivity up to 100 %; specificity up to 95 %) has been reported in the detection of renal masses when proper technique is applied [4,5]

PATIENTS AND METHODS:

This is a cross sectional prospective correlation study of 50 patients with solid or complex renal mass were diagnosed by abdominal ultrasound referred for abdominal multiphasic contrast enhanced abdominal CT examination. 26 female(52%) and 24 male (48%) , age range 3-75 years (median age 51.9). Patients with renal failure, contrast allergy , Patient refuses , unfit for surgical intervention were excluded. Multiphasic contrast enhanced CT was performed on a 64-slice CT scanner (Aquillon 64, V4.51ER010, Toshiba Medical Systems, Tochigi, Japan) the examination begins with precontrast scan including lower chest and abdominopelvic areas for assessment of exact renal lesion site, density, size and any metastasis. figure (1)A. Then a bolus of 50-120 milliliter (according to body weights1ml per kg body weight) of non-ionic iodinated contrast medium (omnipaque 350 mg/ml) was administered intravenously by using automatic pressure injector at a rate of 3ml/s followed by 30ml of normal saline flush. The three postcontrast phases as a sequence:

1. Arterial phase (corticomedullary phase) CMP at 40−70 s, figure (1)B .
2. Venous phase (nephrographic phase) NGP at 80−100 s, figure (1) C.
3. Delayed phase (excretory phase) EP at 120 s, figure (1) D.

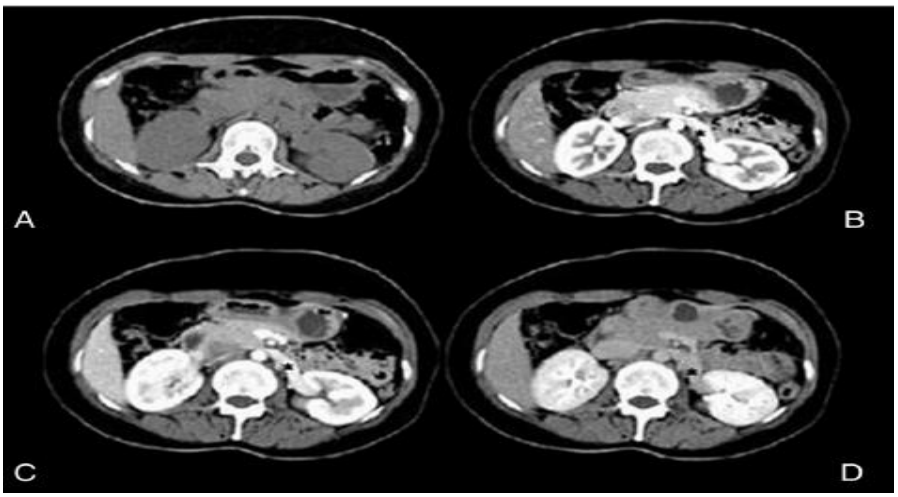

Figure 1: The CMP corticomedullary phase (B) has the best cortical enhancement with lowest medullary enhancement. Almost homogenous nephrogram is seen in both nephrographic (C) and excretory (D) phases.

All CT scan images were reviewed by single radiologist, providing mass dimensions, mass margins, presence or absence of fat, calcification or central scar, morphometric mass description according to R.E.N.A.L nephrometery score (Radius, Exophytic/Endophytic properties of tumor, Nearness of tumor deepest portion to the renal collecting system or sinus, Anterior/Posterior, and Location relative to the polar lines) and mass enhancement patterns. The enhancement pattern of mass was classified as homogenous, heterogeneous, or predominantly peripheral. To evaluate the degree of enhancement of a tumor, the attenuation of region of interest (ROI) of 1cm2 was measured within the lesion at each phase, and the means of minimum and maximum values were calculated. The enhanced area was covered as much as possible in the region of interest and the area of calcification, necrosis, and hemorrhage were excluded from the region of interest. The patients were submitted to either partial, radical nephrectomy or Tru cut biopsy of the mass according to tumor characteristics.

The histopathological analysis of specimens done by expert histopathologist according to World Health Organization 2016.The mean enhancement values of renal masses correlated with their histopathological types and subtypes. Data Were entered and managed by using two programs , the statistical package for social sciences (SPSS) , version 25, 2017 and Microsoft office excel program, 2010. Data were summarized and presented as mean, standard deviation, frequencies and percentage

RESULTS:

The pattern of enhancement was homogenous in 19 (38%) patients and Non-Homogenous in the remaining 31 (62%) patients.

Regarding the correlation of Hounsfield attenuation of renal masses with their histopathological results, Table (1), the precontrast density was not statistically significant among all histopathological types (p.value=0.82). In CMP, mean mass enhancement of chromophobe RCC, clear RCC and AML were significantly higher than that of papillary RCC, Wilm´s tumor and other types (p.value = 0.014), while they were insignificantly different between each other's. In NGP, patients with AML have significantly higher mean mass enhancement than those of all other types (p.vaue=0.013).

Furthermore, in EP, also mean mass enhancement in AML patients was significantly higher than that of patients with all other histopathological types (p.value=0.042).

Table 1: Correlation of mean mass Hounsfield values in different phases with histopathology.

Histopathology	Native HU value	CMP corticomedullary phase HU value	NGP nephrographic phase HU value	EP excretory phase HU value
Clear RCC	34.3	109.3	80.9	68.5
Papillary RCC	28.8	48.8	65.8	54.0
Wilms	37.3	55.0	63.7	62.3
Chromophobe RCC	37.0	121.5	105.5	82.0
AML	33.0	117.0	145.0	120.5
Other*	37.3	85.3	69.7	65.3
P. value among types (ANOVA)	0.82	0.014	0.013	0.042

From other point of view, figure (2) demonstrates the pattern of enhancement of clear RCC on multiphasic CT imaging, figure (3) shows the pattern of enhancement of papillary RCC and figure (4) shows the pattern of enhancement of chromophobe RCC and other tumors.

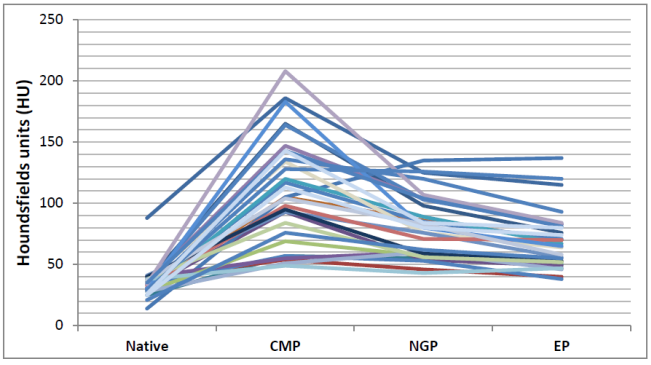

Figure 2: Pattern of enhancement on multiphasic CT imaging of clear RCC masses.

Regarding the enhancement patterns of the renal lesions, there were different patterns of enhancement seen in this study; these patterns can be divided into three different types including:

1) Early (mainly in CMP) rapid high attenuation with rapid washout in the EP was indicative of ccRCC as seen in figure (2).
2) Delayed progressive enhancement with delayed washout with relatively low levels of peak enhancement and little changes in attenuation from phase to phase with the peak enhancement seen in NP, this was seen with pRCC subtype as seen in figure (3).
3) Slowly rising enhancement with presence of plateu with delayed washout can be regarded as intermediate pattern, seen with chRCC subtype and AML. As seen in figure (4).

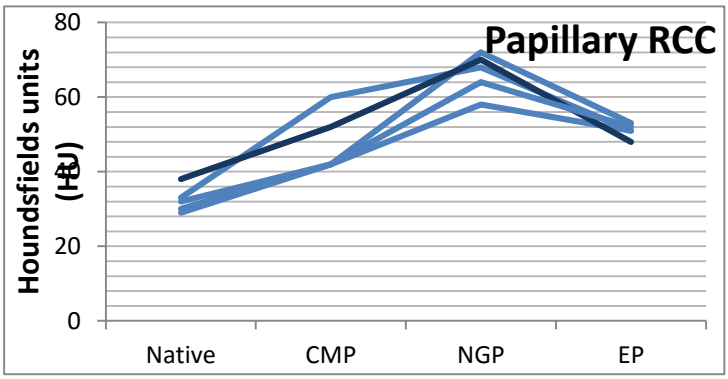

Figure 3: Kinetic curve of papillary RCC in multiphasic CT.

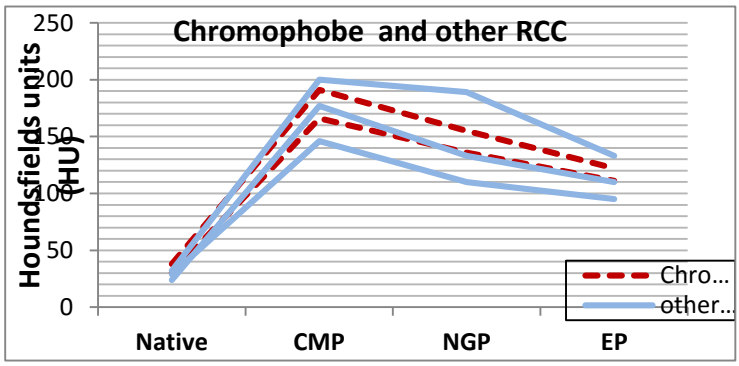

Figure 4: Kinetic curve of Chromophobe and other RCC in multiphasic CT imaging.

For assessment of validity of multiphasic CT imaging to predict and differentiate between the different renal masses, the receiver operating characteristics (ROC) curve was performed for PMC density of mass in prediction of Clear RCC masses, the ROC analysis revealed that CMP was good predictor for clear RCC where area under the curve (AUC = 0.863) with a sensitivity of 82.1%, specificity of 80% and accuracy of 81%, (Figure 5)On the other hand NGP, was also good predictor and can differentiate clear RCC masses than other malignant types, (AUC = 0.890), and it was moderate predictor for papillary RCC (AUC = 0.624), and poor predictor for Chromophobe RCC (AUC = 0.563), and failed to predict other types of RCC (AUC = 0.415), (Figure 6).

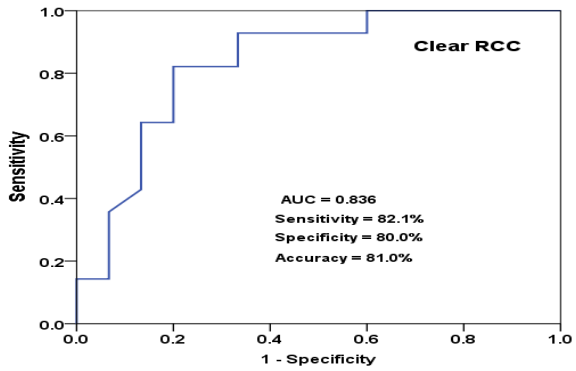

Figure 5: ROC curve for the validity of CMP Density NGP of mass in prediction of Clear RCC masses between types RCC masses.

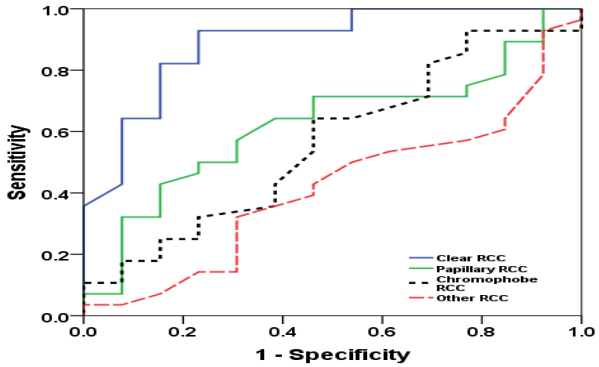

Figure 6: ROC curve for the validity of CT phase in differentiation.

DISCUSSION:

The classification of renal cell carcinoma is based mainly on microscopic appearance of the tumor and genetic abnormalities. Each subtype is associated with a different prognosis and tumor behavior. Patients with papillary renal cell carcinoma or with a chromophobe renal carcinoma have a higher 5 year survival than those with clear cell subtype renal carcinoma of the same stage [(6)]. Multiphasic CT imaging can be helpful in differentiation of RCC subtypes and identifying benign vs. malignant renal tumors[(7)].The current study found that the mean attenuation of renal lesions was not affected by the age or gender of the patients, laterality, location, density appearance on precontrast phase, pattern of enhancement or pattern of growth of lesions (p.value > 0.05). These findings are comparable to the findings of Kim et al study which showed that the demographic distributions were not significantly different among ccRCC, pRCC and chRCC (p > o.05) but his study noticed that the enhancement pattern is the most useful parameter in differentiating RCC subtypes ($p < 0.05$) which is not consistent with our findings[(6)].We found that the unenhanced phase has no statistically significant difference in mean attenuation of renal lesions (p = 0.82). Kim et al study shows that the mean attenuation of fat poor AML in the unenhanced phase was significantly higher than that of ccRCC (36.5 HU vs. 27.3 HU, p=0.02)(6).In CMP, mean attenuation of ccRCC, chRCC and AML (109.3 HU, 121.5 HU and 117 HU respectively) were significantly higher than that of pRCC, wilm´s tumors and other types (48.8 HU, 55 HU and 85.3 HU respectively) (p = 0.014), but there were no significant difference between each other. Kim et al study findings are consistent with our findings in that the mean attenuation of ccRCC is significantly higher than that of pRCC (p.value = 0.003). His study revealed that the mean attenuation of ccRCC is significantly different from that of chRCC (p = 0.005) and fat poor AML (p = 0.02)(6).Sureka et al study noticed that ccRCC and chRCC showed greater mean attenuations (116.11±27.08 HU and 103.00±22.48 HU) respectively in CMP when compared to pRCC mean attenuation

(78.50±12.49 HU) which not consistent with our findings [11] .while Chen et al study concluded that the mean attenuation of ccRCC was significantly higher than that of pRCC in CMP (93 HU vs. 51 HU, p < 0.01)[8] which is consistent with our study findings.

Chen et al study manifested that the mean attenuation of ccRCC was significantly higher than that of pRCC in nephrographic phases (111HU vs. 76 HU, p < 0.01) [8] which is not consistent with our study findings.

In our study, EP showed that the mean attenuation of AML was significantly higher than that of all other types (p.value =0.042), which is consistent with choi SK et al study finding [9].

Regarding the enhancement patterns of the renal lesions, there were 3 different patterns of enhancement seen in this study; these patterns can be divided into three different types including:

1) Early (mainly in CMP) rapid high attenuation with rapid washout in the EP was indicative of ccRCC as seen in figure [2], this agree with phillip M. pierorazio et al[7] study that found the ccRCC shows rapid enhancement in CMP.
2) Delayed progressive enhancement with delayed washout with relatively low levels of peak enhancement and little changes in attenuation from phase to phase with the peak enhancement seen in NP, this was seen with pRCC subtype as seen in figure (3). This also has been demonstrated by Alshumrani et al(10) that shows all pRCCs enhanced by ≤ 32 HU in the NP.
3) Slowly rising enhancement with presence of plateu with delayed washout can be regarded as intermediate pattern, seen with chRCC subtype and AML. As seen in figure (4). This is consistent with Zhang et al study that concluded that ccRCC and oncocytoma were hypervascular leading to rapid and early enhancement after examination of 198 patients with solid renal lesions and found pRCC was mostly hypovascular leading to low and delayed levels of enhancement, and that chRCC and AML enhanced moderately and it was correlated with intermediate levels of vascularity [11].

The presence and demonstration of fat attenuation density in the renal lesion is virtually diagnostic of AML[12].One case of middle age female which is histopathologically proved to be lymphoma, dynamic CT scan showed the lesion to be homogenously enhancing in the CMP with retaining enhancement even in the excretory phase, which is consistent with Urban BA et al study finding[13].Other lesions among the included masses are three pediatric patients with histopathologically proved wilm´s tumors, these lesions are hypovascular showing slow pattern of enhancement during dynamic examination, this is cosistent with Fishman EK et al study at 2013[14] which reported that wilm´s tumors show heterogenous low enhancement .

CONCLUSION:

Muliphasic contrast enhanced CT is reliable modality of imaging in differentiating clear RCC from non- clear RCC. -clear cell RCC can differentiated from papillary subtype because clear subtype show maximum enhancement at corticomedullary phase with rapid wash out while papillary subtype show delay progressive enhancement with delayed wash out with relatively low level of peak enhancement at nephrogenic phase.

-AML and chromophobe RCC with other subtypes show moderately rising enhancement so difficult to differentiate from each other

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