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Magnetic Resonance Imaging with Diffusion Weighted Sequence in Comparison with Multiphase Contrast Enhanced Computed Tomography in Characterization of Renal Masses

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Abstract: Objective: To evaluate the additive value of the magnetic resonance imaging with diffusion weighted sequence in the characterization of the renal masses comparable with multi-phasic contrast enhanced computed tomography. **Patient and method:** This study was conducted on 50 patients; including indeterminate solid or cystic renal lesions detected by ultra sound or computed tomography, in addition to these lesions 10 simple cysts noted incidentally in the study population were included in the study. The data were collected during 26 months. CT study was done in all cases using 4, 16 and 64 detectors In 40 cases the study was performed as pre-contrast and multi-phasic post contrast study while in 10 cases, the study was done as non-contrast study only due to low creatinine clearance Multi-phasic CT was done as four-phase CT imaging that included an unenhanced scan and the evaluation of the corticomedullary phase (CMP), nephrographic phase (NP), and excretory phase (EP). Renal magnetic resonance imaging (MRI): All patients received 1.5 ml/kg of intravenous nonionic contrast material. Images were acquired on a 1.5-tesla whole-body scanners using body phased array coil. **Results:** Renal lesions in the current study (n=82) were subdivided based upon the final diagnoses into 58 renal tumors (70.7%) (Including 10 benign and 48 malignant tumors), 14 non tumorous lesions (17.1%) (Including 2 solid (post-operative cortical defect) and 12 cystic lesions) and 10 simple cysts (12.2%) which were incidentally noted in the study population. The study was performed on 58 cases including 36 males (62.0%) and 22 females (38%). The mean age is 55.24 ± 15.5 years ranging from 4 years to 82 years. (Table 14) Among the 82 lesions included in the study, 42 lesions were right sided representing 51.2% and 40 lesions were left sided representing 48.8 %. The lesions in the current study were variable in size; their maximum dimensions ranged from 1 to 15 cm with a mean of 5.19 ± 3.2 cm. The final diagnosis has been reached by excision biopsy in 44 lesions (53.7%), core biopsy in 11 lesions (13.4%), fine needle aspiration cytology (FNAC) in 5 lesions (6.1%) and in the remaining 22 lesions (26.8%) the diagnosis was based on the radiological findings supported by clinical data with 6 of these lesions needed 3 months follow up with monitoring response to medical treatment in cases diagnosed radiologically as abscesses or hemorrhagic cysts while in the other 16 cases the diagnosis was clear radiologically by the presence of fat or in Bosniak I and II cysts, these cases needed no follow up or further assessment. Renal insufficiency was found in 15 cases, two of them were known patients with adult poly cystic kidney disease, in this group CT and MRI were done without contrast administration. Tuberous sclerosis syndrome was found in one case with bilateral renal angiomyolipomas this patient also had multiple brain tubers, cystic lung disease and fatty hepatic lesions. Birt-Hogg-Dube syndrome was found in a single case with multiple oncocytomas, the patient had also multiple benign facial cutaneous lesions.
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Keywords: Ct contrast enhananced, Diffusion weighted MRI, Renal masses.

1. Introduction

The great majority of renal masses are found incidentally as a result of the use of computed tomography (CT), ultrasonography (US) and magnetic resonance (MR) imaging.

1. Ultrasonography may incidentally detect a cystic or solid renal mass. CT and MR1 are the primary investigative tools for diagnosing, characterizing and staging renal masses. The density or intensity on unenhanced imaging and the enhancement characteristics have been used in determining the nature of renal masses. For cystic renal lesions, the Bosniak classification system stratifies the CT or MR appearances with the risk of malignancy.

2. More recently, differences in enhancement characteristics of clear cell renal cancer from papillary renal cell cancer have been reported**.**

3. Diffusion of water molecules is reduced in the intracellular space compared with the extracellular

space. Thus, highly cellular tumors may be more likely to have restricted diffusion than less cellular tumors. This concept is supported by findings in brain, prostate gland, and breast neoplasms.

4. Recent studies assessed the usefulness of DWI in evaluating renal masses notably in patients who have renal functional impairment would be of particular help in evaluating such patients. **5** Moreover, diffusion-weighted (DW) MR imaging with apparent diffusion coefficient (ADC) measurement can be used to characterize non-fat-containing T1 hyperintense renal lesions; mean ADC is significantly lower in renal cell carcinomas (RCCs) than in benign hemorrhagic or proteinaceous cysts. The sensitivity and specificity of DW imaging are equivalent to those of enhancement ratio measured with contrast-enhanced MR imaging; however, the sensitivity of DW imaging is lower than that of image subtraction for the diagnosis of RCC**.**

6. For many years, RCC was considered as a single pathologic entity. Today, the term RCC embraces a heterogeneous group of renal carcinomas, all of which are derived from the renal tubular epithelium but each with distinct clinical, pathologic, phenotypic, and genotypic features.

7. Staging of RCC: In staging RCC, the goal of any imaging study is to identify patients who have a resectable tumor and can be cured by means of surgical intervention.

2. Materials and Methods:

This study was conducted on 50 patients All patients with renal masses included in this study were subjected to the following:

- Thorough history taking about hematuria, lion pain, renal insufficiency and family history of malignancy.
- Complete physical examination with special emphasis on signs of renal failure and abdominal masses.
- Laboratory investigations including.

1. Urine analysis for hematuria.
2. Calculation of the estimated creatinine clearance using Cockroft–Gault equation.

CT study was done in all cases using 4, 16 and 64 detectors row helical scanners (light speed GE Medical Systems, Somatom – Seimens medical system and Aquilion - Toshiba Medical Systems). CT images were obtained during patient breath holding with the following parameters: 120 kVp, 200–400 mA (depending on patient size), section thickness and interval of 8 and 6 mm respectively with reconstruction thickness and interval ranging from 2.5 and 1.25mm to 1 and 0.8 mm respectively according to the device used.

In 43 cases the study was performed as pre-contrast and multi-phasic post contrast study while in 15 cases, the study was done as non-contrast study only due to low creatinine clearance.

Multi-phasic CT was done as four-phase CT imaging that included an unenhanced scan and the evaluation of the corticomedullary phase (CMP), nephrographic phase (NP), and excretory phase (EP). All patients received 1.5 ml/kg of intravenous nonionic contrast material.

Images were acquired on a 1.5-tesla whole-body scanners using body phased array coil. Three devices were included in the study as follow:

- Magnetom, Avanto by Siemens, Erlangen, Germany: (39 cases)
- Achieva 1.5T SE - Philips (8 cases)
- GE Signa Horizon LX 1.5T Scanner: (3 cases)

Image Analyses:

The CT and MRI images were reviewed at a picture archiving and communication system (PACS) monitor, at which it was possible to measure tumor diameter, attenuation in a particular region of interest, manipulate the image size and window level and multi-planner reconstruction.

Tumor characterization CT:

Pre contrast assessment

For detection of calcification, fat attenuation and initially hyper-dense lesions. Pre contrast attenuation was used as a base line measurement to assess the degree of enhancement.

Assessment of enhancement

The degree of enhancement of each phase was measured as a figure number which is the mean attenuation value of the region of interest. In cases of heterogeneous lesions with variable enhancement values, multiple regions of interest were placed over the enhancing areas and the highest value was selected.

Magnetic resonance imaging

(a) Conventional T1 (Fat saturated) and T2-weighted sequence:

Signal intensity of the lesions was analyzed for assessment of the nature of different components of the lesion.

The tumors signal intensity was compared to the signal intensity of the renal parenchyma (Tumor/ parenchymal T2 signal intensity ratio) and the results for solid renal masses were compared with each other. T2 weighted sequence was used as well in assessment of internal heterogeneity of the lesions.

Non contrast volumetric fat saturated T1 sequence was used as the base line to assess the degree of enhancement. This sequence is volumetric sequence that allowed multi-planner imaging as well as

maximum intensity projection images for vascular mapping (in post contrast sequences).

(b) In-phase and out-of-phase sequences:

For estimation of the lipid contents within the examined lesions, this was done either subjectively by visual comparison of their signal intensity in both sequences or mathematically through assessment of the following indices.

(c) Assessment of diffusion restriction and ADC value:

Restricted diffusion was considered when the lesion brightness persists at b value of 800 and its ADC map shows low intensity and low ADC value.

Comparison between CT and MRI in characterization of renal masses as benign versus malignant:

All lesions included in the study were prospectively characterized into benign versus malignant by multi slice CT, conventional MRI with diffusion weighted imaging (DWI), dynamic contrast enhanced MRI (DCEMRI) and full MRI study with DCEMRI and DWI. The accuracy of each method in characterization was calculated and compared with the accuracy of the other methods.

Statistical analysis:

Statistical Package for the Social Science version 10; Chicago, Ill) program software package for windows. Univariate analyses including: t-test and Mann Whitney test, Kruskal Wallis test and ANOVA test were used to test the significance of results of quantitative variables. The P value was considered significant if 0.05 or less at 95% confidence interval. Receiver operating characteristic curve was drawn to determine the cutoff point with highest sensitivity and specificity that used to differentiate malignant from benign renal tumors and different subtypes of RCC. The sensitivity, specificity, accuracy, positive predictive value (PPV), negative predictive value (NPV), and the area under the curve was computed from the curve.

3. Results:

Renal lesions in the current study (n=82) were subdivided based upon the final diagnoses into 58 renal tumors (70.7%) (Including 10 benign and 48 malignant tumors).

Table 1: Final diagnosis of the lesions and the method of diagnosis

Method / Final Diagnoses	Excision biopsy	Core biopsy	FNAC	Clinical and radiological diagnosis	Clinical diagnosis and follow up
RCC (n=37)	34	3	-	-	-
Other malignant renal tumors (n=11)	4	5	2	-	-
Benign renal tumors (n=10)	6	1	-	2	1
Non tumerous lesions (n=14)	-	2	3	4	5
Simple cysts	-	-	-	10	-
Total (n=82)	44	11	5	16	6

Table 2: Non contrast CT attenuation among papillary and non-papillary RCC lesions.

Parameter	Lesions		Significance
	PRCC	Non PRCC	
Min-Max	30-45	20-37	Z=3.045
Mean±SD	35.9±5.7	28.8±3.8	P=0.002*

Table 3: Attenuation values of different solid renal lesions (n=42) at various post contrast phases.

Pattern of enhancement / Attenuation value		Attenuation (HU)		
		CMP	NP	EP
Wash out pattern (n=26)	CCRCC (N=18)	103.6±41.9	79.3±27.3	54.4±15.56
	Oncocytoma (N=3)	135 ± 13	125±8.9	82.3±23.7
	CHRCC (N=2)	83.5	73.5	46.5
	Solid portion of lipid rich AML (N=3)	93.7±2.5	66.3±10.9	40±8.6
Prolonged enhancement pattern (n=14)	PRCC (N=6)	48.1 ± 10.2	61.6 ±15	53.8±11.5
	RCC unclassified (N=1)	37	56	50
	Lipid poor AML (N=1)	33	36	50
	Lymphoma (N=1)	55	74	70
	TCC (N=2)	78.5	81	62
	Hemangioendothelioma (N=1)	70	82	90
	Metastases (N=1)	70	76	70
	Neoplastic renal vein thrombus (n=1)	68	60	53
Gradual enhancement pattern (n=2)	Wilm's (N=1)	70	84	96
	Hemangioma (N=1)	60	75	92

Table 4: MRI opposed sequences parameters among malignant and macroscopic fat containing lesions.

MRI in/out sequence	Lesions		Significance
	Malignant	Fat containing	
SI index in opposed phase (%)			Z=2.475 P=0.011*
Min-Max	-20 – 19	1-88	
Mean±SD	5.3±7.8	58.2±40.1	
Tumor to spleen ratio (%)			Z=2.406 P=0.013*
Min-Max	-19 – 16	-98.0 – -1.0	
Mean±SD	-5.6±8.4	-55.8±39.9	

Table 5: Classification of renal cysts (n=12) by contrast enhanced MRI following Bosniak classification (These cysts proved to be benign cysts)

Cyst type		Criteria	Number	Percentage (%)
Benign cysts	**Bosniak 1**	- No enhancement - Fluid signal intensity - Thin wall - No septations - No enhancement	6	91.6
	Bosniak II	- No enhancement - Altered fluid signal - Few thin septations	5	
Indeterminate cysts	**Bosniak IIF**	- No enhancement - Multiple internal septae	0	8.4
	Bosniak III	- Mural or septal enhancement	1	
Malignant cysts	**Bosniak IV**	- Intra cystic enhancement	0	0

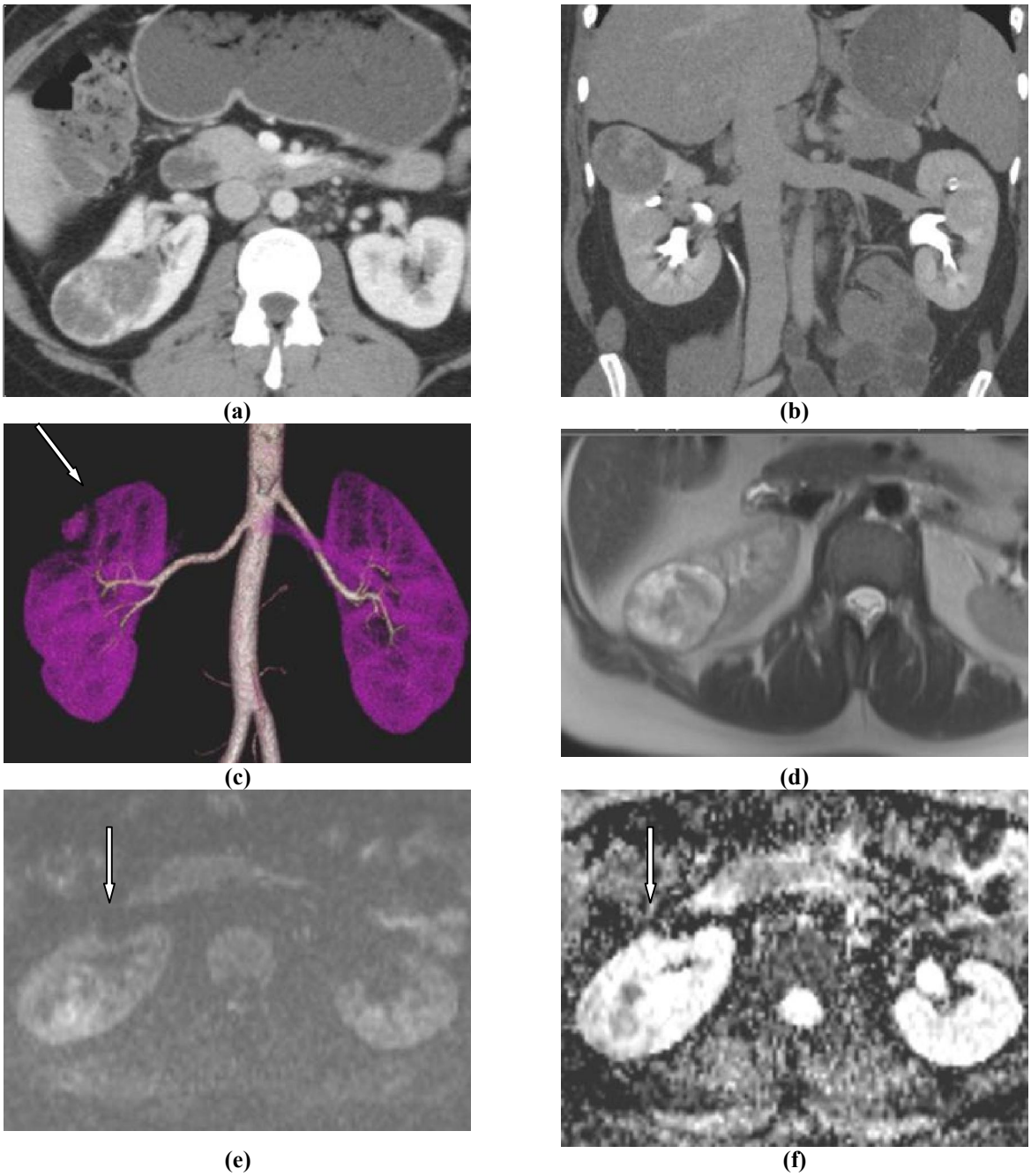
Table 6: ADC and L/P ADC ratios among various renal lesions included in the current study subdivided into malignant tumors, benign tumors, complex cysts and simple cysts (with exclusion of abscesses and late sub acute hematomas)

Diagnosis / ADC	Malignant	benign tumors	Complex cysts	Simple cysts	Significance
ADC value ($\times 10^{-3}$ mm^2/s)					
Min-Max	0.5-1.3	1.1-2.7	1.7-2.7	2.5-3.0	$^{KW}X^2$=49.249 P<0.0001*
Mean±SD	0.9±0.2	1.7±0.5	2.2±0.4	2.8±0.2	
L/P ADC ratio					
Min-Max	0.3-0.72	0.67-1.5	1.0-1.5	1.5-1.8	$^{KW}X^2$=47.114 P<0.0001*
Mean±SD	0.49±0.1	0.9±0.2	1.3± 0.2	1.6±0.1	

Table 7: CT and conventional MRI parameters used in the current study as indicators of malignancy and benignity in solid lesions.

Values / Parameter	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Malignant indicators				
Internal heterogeneity				
Multi-phasic CT	70.6%	100%	100%	40%
DCEMRI	72.7%	100%	100%	66.6%
Conventional MRI	73.3%	66.6%	91.6%	85.7%
Benign indicators				
Fat content (In absence of intra lesional degeneration)				
CT and MRI	60%	100%	100%	92%

Case 1

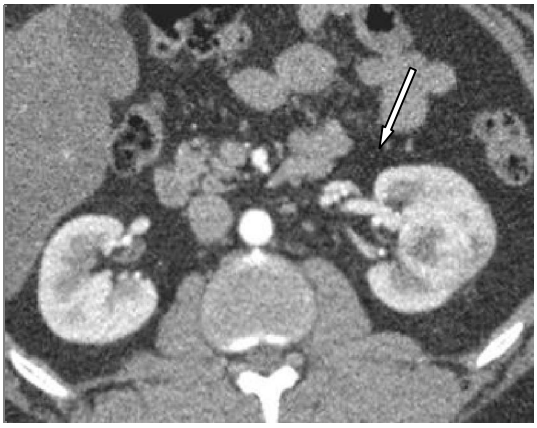


(a) **(b)** **(c)** **(d)** **(e)** **(f)**

Case 1: **Pathologically proven clear cell renal cell carcinoma in a 42 years old female with incidental discovery of solid renal lesion during a checkup abdominal ultrasound examination**

Multi-phasic CT scan at the cortico-medullary phase **(a)** and excretory phase **(b)** reveal a heterogeneous partially exophytic mass lesion bulging from the upper pole of the right kidney with well defined outlines. The lesion shows early enhancement at the cortico-medullary phase with wash out in the excretory phase. **(c)** Volume rendered image reformatted from the arterial phase scan shows the lesion as a filling defect within the enhancing renal parenchyma (arrow). **(d)** Axial T2 weighted sequence demonstrates a well defined hypo-intense capsule with internal heterogenicity of the lesion. The areas of T2 hypo-attenuation are compatible with the enhancing portion of the lesion at CT. **(e)** Diffusion weighted sequence *b* 800 mm ^{2} / sec and ADC map **(f)** reveal areas of restricted diffusion (asterisk) with low ADC reaching 0.9 x10 $^{-3}$ mm ^{2} / sec.

Case 2



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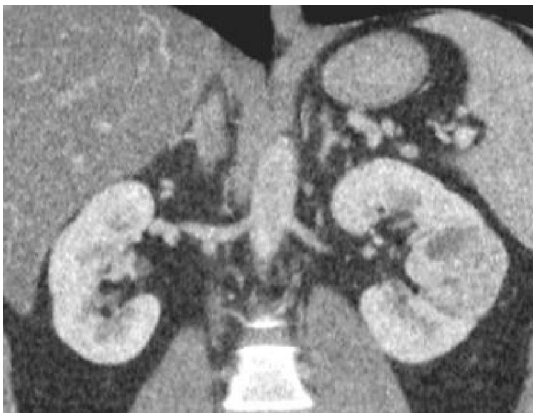

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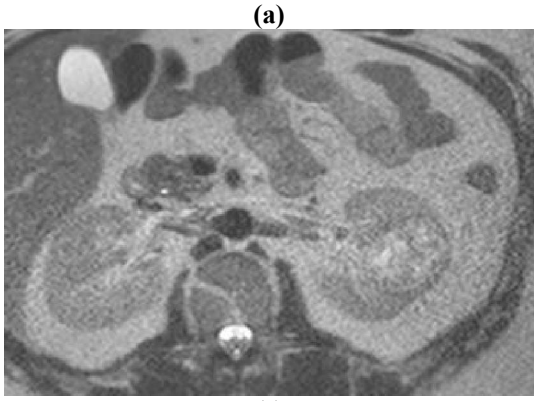

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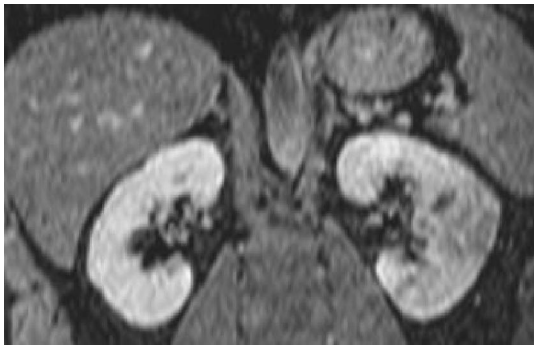

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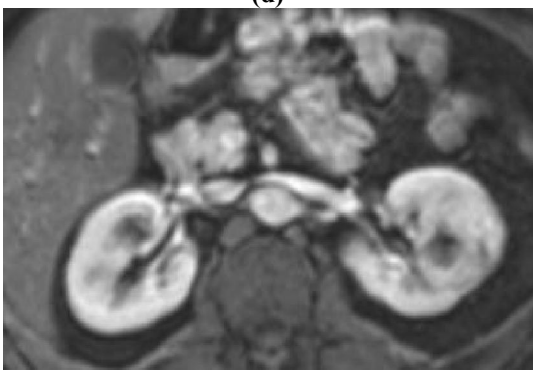

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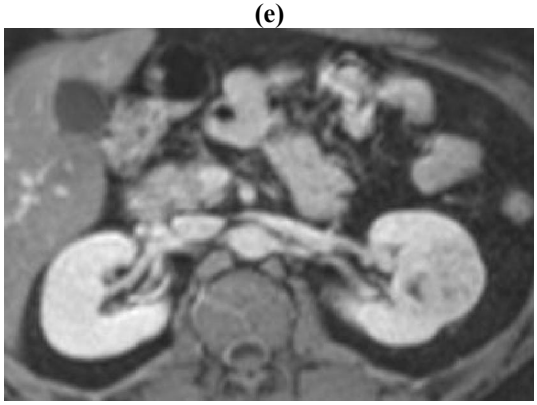

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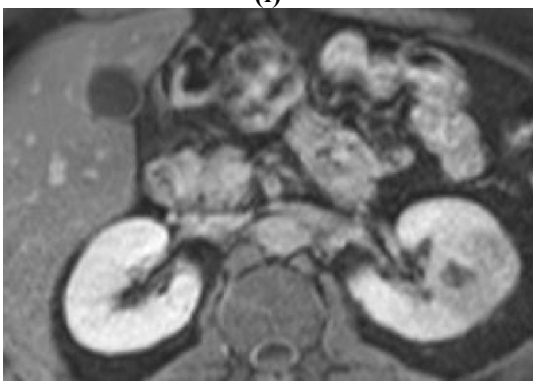

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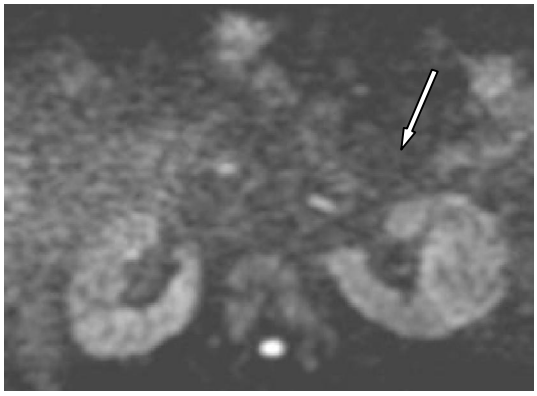
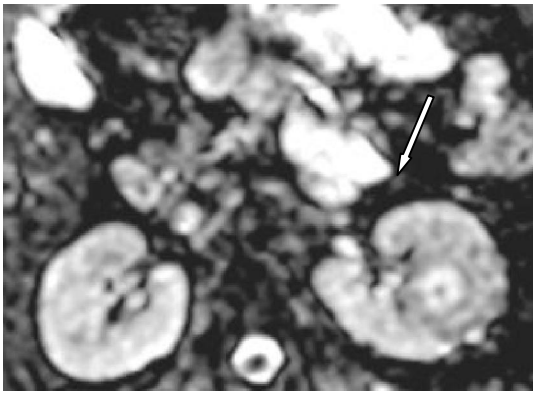
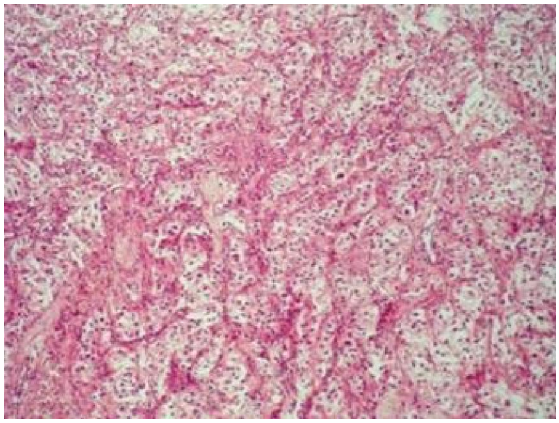


(i)



(j)



(k)

Case 2: Pathologically proven clear cell type renal cell carcinoma in a 36 years old male patient with an incidentally discovered left renal lesion during an ultra-sound examination for elevated liver enzymes

Multi-phasic CT study at cortico-medullary phase **(a)** and nephrographic phase **(b)** reveals a well defined lesion seen originating from the mid portion of the left kidney (arrow in (a)) with mild internal heterogenicity. The lesion shows early enhancement in the cortico-medullary phase and wash out in the nephrogenic phase and excretory phase (not shown). Axial T2 weighted sequence **(c)** and coronal T2 fat saturated sequence **(d)** reveal heterogeneous signal of the lesion.

Multi-phasic dynamic contrast enhanced MRI at pre-contrast **(e)**, cortico-medullary **(f)**, nephrogenic **(g)** and delayed **(h)** phases confirms the enhancement pattern noted in CT with early enhancement followed by enhancement wash out. Diffusion weighted sequence *b* value 800 mm ^{2} / sec **(i)** and ADC map **(j)** reveal restricted diffusion (asterisk) with low ADC value of 1.2 x10 $^{-3}$ mm ^{2} / sec. Photomicrograph (powerx100) of the lesion after surgical excision reveals trabeculae formed of clear cells with prominent fibrovascularstroma.

4. Discussion:

- Based on the current study data, multi-detector CT and 1.5 MRI tesla offered precious information in the assessment of renal lesions, these information helped in characterization of renal masses as benign versus malignant, in differentiation between RCC subtypes and in staging of RCC.
- In the current study, through assessment of renal masses by non-contrast CT, PRCC lesions (n=7) showed higher pre contrast attenuation values than other RCC sub types (n=27) (35.9±5.7 HU versus 28.8±3.8 HU with P=0.002). In the literature, matching results were found by El-Esawy et al (208) and Fujimoto et al **9** who found that CT high attenuation in tumors has been shown to correlate with PRCC.
- A single lipid-poor angiomyolipoma (AML) lesion was included; it showed high pre-contrast attenuation value (38 HU) without any detectable fat radiologically. In the literature, Kim et al (52) found that 53% of AMLs with minimal fat showed high attenuation while 22% of RCCs (regardless their subtype) also showed high attenuation on unenhanced scans. In other studies **10** lipid poor AMLs showed high pre contrast attenuation, however, these studies included limited number of cases.

- Based on the current study data in assessment of the enhancement pattern and the degree of enhancement, the renal tumors can be classified into two groups; The 1st group included the lesions that enhanced avidly in the corticomedullary phase (CMP) with wash out in the following phases (n=26). This group included four tumor types which were oncocytoma, CCRCC, chromophobe renal cell carcinoma (CHRCC) and lipid rich AMLs. The 2nd group included the remaining solid renal lesions (n=16), these lesions showed lower degree of enhancement and either gradual or prolonged enhancement pattern.
- In the literature, matching results were described by Chai Jung et al who found a significant difference in enhancement between the clear cell and papillary types in the CMP ($P < 0.01$) and between clear and non-clear cell types in the NP ($P < 0.05$).
- In other studies, Kim et al found that CCRCC enhanced to a mean of 149 HU ± 46, whereas PRCC enhanced to a mean of 91 HU ± 12 and CHRCC enhanced to 90 ± 14 while Wang et al **11** found that the degree of enhancement between the papillary subtype and the clear cell subtype is due to differences in the intra-tumoral vascularity measured in terms of micro-vessel density.
- The current study results are matching with Kim et al who found in their study on 113 renal lesions that in tumors less than 3 cm in diameter, a heterogeneous or predominantly peripheral enhancement pattern was noted in 10 patients (56%) with CCRCC, whereas 4 of 5 PRCCs and all CHRCCs showed homogeneous enhancement. In tumors 3-7 cm in diameter, CCRCC (93%) and PRCC (88%) showed predominantly heterogeneous or predominantly peripheral enhancement pattern, whereas, CHRCCs (67%) showed homogeneous enhancement. In tumors greater than 7 cm in diameter, the frequency of homogeneous enhancement was higher in CHRCC (63%) than in CCRCC (6%) ($p = 0.000$).
- Matching results were noted in the literature by Kim et al who found that 8 out of 10 renal oncocytomas and only one (which was proven to be CHRCC) out of 88 RCCs showed segmental inversion during CMP and excretory phase while McGahan et al**.12** found in their study performed on 16 oncocytomas that the most common feature identified (in 8 lesions) was a slightly heterogeneous mass that became homogeneous on the later phase of CT, 3 tumors had a central region of low density and 2 tumors showed distinct segments of variable degrees of enhancement with 1 of those tumors having segmental enhancement inversion.
- Matching results were described by Oliva et al **13** who found that most PRCCs on T2-weighted images in their study were hypo-intense, with SI ratio of 0.67 ± 0.2, whereas most CCRCCs were hyper-intense, with signal intensity ratio of 1.41 ± 0.4. A tumor T2 signal intensity ratio of ≤ 0.66 had a specificity of 100% and sensitivity of 54% for PRCC. They also found that other solid renal tumors also can be T2-hypointense, such as angiomyolipoma with minimal fat and solitary fibrous tumor of the kidney.
- By calculation method, the current study found that lesions with gross fat (n=4) showed higher signal intensity index ($P=0.011$) and lower tumor-to-spleen signal intensity ratio ($P=0.013$) in comparison with RCCs regardless of their subtype. (Page 62) The other three lesions (containing minimal fat) as well as a single lipid-poor AML with no detectable fat showed signal intensity indices and tumor-to-spleen signal intensity ratios similar to RCC.
- In the literature, mismatching results were reported by Kim et al **14** who found that AMLs with minimal fat can be differentiated from RCC when the signal intensity index is greater than 25% and the tumor-to-spleen ratio is ≤ –32%, with a specificity of 93% and sensitivity of 97%.
- In the current study DWI was able to differentiate between CCRCC from other RCC subtypes where the former showed higher ADC value (1.1±0.2 ranging from 0.6±1.4× 10−3 mm2/s versus 0.7±0.1 ranging from0.5-0.8× 10−3 mm2/s) and T/P ratio (0.56±0.11versus 0.4±0.05) with $P<0.0001$.
- No significant difference between mean ADC values of clear cell RCCs and those of non CCRCCs was found in another study including 17 malignant lesions by Kim et al**15** using b values of 0 and 400 sec/mm2.
- In one case of PRCC, black out effect was noted with low signal in DWS and low ADC value, we attribute this to susceptibility artifact caused by abundant hemosidrin deposit in PRCC lesions which was described by Silverman et al 16.
- In the current study staging of RCC was done by TNM staging. CT and MRI failed to directly asses the continuity of renal capsule and peri-nephric fascia and staging was dependant on the indirect signs with the overall frequency of peri-nephric changes, venous invasion and lymphadenopathy were lower than those documented in previous reports. **17** This might be attributable to the fact that the increased use of cross sectional imaging has resulted in the earlier detection of renal cell carcinoma than in the past. **18.**
- In the literature, we did not find previous studies comparing between MRI with DWI and MDCT, further studies using a larger number of patients are required to justify the current study results.

5. Conclusions

• In cross sectional imaging using CT and MRI; gross fat in absence of calcification or internal cystic degeneration is the most reliable sign of benignity of the renal lesion while heterogeneity of enhancement is the most reliable sign of malignancy. If the enhancement heterogeneity is coupled with rapid wash in wash out enhancement pattern, clear cell renal cell carcinoma is highly suggested.

• Enhancement of renal lesions regardless its pattern in CT and MRI denotes its solid nature however; it does not necessary means malignancy.

• Contrast enhanced MRI is better than CT in assessment of enhancement in cystic renal lesion. When a solid lesion enhances avidly on CT, contrast enhanced MRI will not have an additive value in characterization of the lesion however; it is helpful in lesions with equivocal CT enhancement or equivocal diffusion restriction.

• Diffusion weighted sequence can discriminate between renal cell carcinoma subtypes with significantly higher ADC value of clear cell renal cell carcinoma than papillary and chromophobe subtypes.

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