Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 6, 2021, Pages. 15004 - 15013
Received 25 April 2021; Accepted 08 May 2021.

Added Value of Apparent Diffusion Coefficient and Diffusion Weighted Imaging in Characterization of Renal Masses

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Abstract

Background: The detection of renal masses has been recorded in a marked way over the past years with the increasing use of radiological imaging modalities, majority of renal masses are renal cell carcinoma (RCC).Diffusion Weighted (DW) Magnetic resonance imaging (MRI) can help in differentiating benign from malignant lesions.

Aim of the study: This study aimed to improve characterization of renal masses using magnetic resonance diffusion weighted imaging and apparent diffusion coefficient (ADC) values, and therefore determining accurate surgical planning and improving patient management.

Patients and methods: This was a cross-sectional study was performed in the period from July 2020 to May 2021 in Zagazig university hospitals and was conducted on thirty patients having renal masses previously diagnosed with ultrasound and/or computed tomography, referred to the radiology, urology and oncology departments. All patients were subjected to full history taking, radiological examination including: Ultrasonography, Contrast enhanced MRI of the upper abdomen and histopathological correlation of surgical specimens.

Results: There was statistically significant difference in mean of ADC in relation to different types of malignant RCC, while it showed no statistically significant difference in relation to different types of benign renal masses.

Conclusion: This work results demonstrate the potential utility of DW imaging for the characterization of renal masses. Most solid tumors showed restricted diffusion because of their higher cellularity, resulting in restriction of water movement and corresponding high signal intensity on DWI.

Keywords: Renal Cell Carcinoma (RCC), Diffusion Weighted Imaging.

1. Introduction:

The detection of renal masses has risen significantly over the past years with the increasing use of radiological imaging modalities, majority of renal masses are renal cell carcinoma which account for 80 to 85% of primary renal tumors and approximately 3% of all malignancies in adults(1).

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Early diagnosis of renal masses is essential for appropriate management, differentiating benign from malignant renal masses and also identifying masses which need surgical intervention (2).

Magnetic resonance (MR) imaging has advantages over MDCT of being a non-invasive, multi-planar modality, uses no ionizing radiation and can be used in patient with deranged renal function (3).

Application of diffusion-weighted sequences in body imaging had been limited, however with the recent use of faster, more robust sequences, better image quality can be achieved and diffusion-weighted imaging has shown great potential for use in abdominal imaging (3).

DW MRI can help in differentiating benign from malignant lesions and in subtyping of renal malignancies using ADC values (4).

The apparent diffusion coefficient (ADC) gives quantitative information in DW MRI and has been shown to be inversely related to cellularity and grade of neoplasms (5).

We aimed at this study to find out improvement of characterization of renal masses using magnetic resonance diffusion weighted imaging and ADC values, and therefore determining accurate surgical planning and improving patient management.

2. Patients and Methods:

2.1. The current study was conducted cross sectional.study was performed in the period from July 2020 to May 2021 in Zagazig university hospitals and was conducted on thirty patients having renal masses previously diagnosed with ultrasound and/or computed tomography, referred to the radiology, urology and oncology departments .These patients included (13) females and (17) males, the age ranged from 3 years to 72 years old after obtaining the approval of the institutional review board (IRB) of Zagazig University.

2.2.A consent form approved by the committee of human rights in research in Zagazig University was obtained from each participant before the study initiation.

2.3. Patients who were included in this study of any age and both sexes with renal mass previously diagnosed by CT scan or ultrasound.

2.4. All patients who have contraindications for MRI such as patients with:implanted electric and electronic devices, heart pacemakers, insulin pumps, implanted hearing aids, and intracranial metal clips were excluded from the study.

2.5. The patients who met the inclusion criteria and were suitable candidates for the study have been subjected to:

1) History Taking

-Personal history; name, age and sex.
- Positive family history for similar conditions.
- Medical history; presenting symptoms, previous investigations, medical treatment or previous surgical operations.

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2) Radiological examination including:

A: Grey-scale sonography in longitudinal, transverse and oblique planes for ultrasonographic features of the renal mass (solid or cystic, calcification, central degeneration, multifocality and bilateralism) as well as regional lymphadenopathy.

B: Color Doppler sonography:

- Renal vein and IVC for vascular invasion by tumor thrombus.
- Focal lesion to assess the vascularity of the lesion (hypovascular or hypervascular).
- Renal artery for vascular anomalies (AVM, aneurysm, pseudoanurysm).
- Renal parenchyma for focal absence of perfusion.

3) Contrast enhanced MRI of the upper abdomen.

MRI study technique

The MRI was performed at (1.5 tesla) superconductive magnet (Achieva, Philips Medical System) using a surface coil with respiratory triggering.

Patients were lying supine in head first position at complete rest. Hands were placed behind head. All instructions were given to the patient about timing and manner of breath holding.
For morphologic evaluation of the kidneys, respiratory triggered axial and coronal T2-weighted fast spin-echo sequences, axial T2-weighted SPAIR (spectral Attenuated inversion recovery) with fat suppression were initially performed, followed by axial T1-weighted fast low angle shot (FLASH) GRE sequence, and T1-weighted dual-echo in-phase and out-of-phase sequences.

The DWI functional study was performed with a single shot spin-echo echo-planar imaging (SE-EPI) inversion recovery sequence acquired in the axial plane with sensitivity encoding (SENSE) in a single breath-hold with the following parameters:

- TR/TE 8000/58 ms
- EPI factor 53
- FOV/RFOV 320 mm (80%)
- Acquisition matrix 160 , reconstruction matrix 256
- 18 sections with a 7-mm slice thickness, interval 0 mm and two b values (600&800 s/mm2)

Then a dynamic study was performed using 3D isotropic fast-field echo (FFE) T1-weighted sequences with SPAIR fat-signal suppression in the axial plane after intravenous administration of 0.2 mmol/kg of gadolinium diethylenetriaminepentaacetic acid (Gd-DTPA) contrast material with an injection rate of 2.0 ml/s, followed by 20 cc of saline solution with the same injection rate.

Table (1): Diffusion-weighted imaging (DWI) sequence parameters for the magnetic resonance imaging study of kidneys and renal focal lesions

TR/TE	8000/58 ms
EPI factor	53
Thickness/interval	7.0/0.0 mm
FOV/RFOV	80%
Matrix (acq/rec)	160/256
b value	600&800mm2/s
No. of sections	18
Scan length (s)	30

Qualitative and quantitative image analysis was performed with the selection of regions of interest

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(ROIs) on the ADC map generated for each of the 18 slices obtained on the basis of the algorithm represented by the following equation:

ADC mm2/s = [1/1000 X ln (IS (b0) /IS (b1)]

Where IS (b0) and IS (b1) are the signal intensities obtained with two different b values (0 & 1000).

Measurement of the mean and SD of ADC values for focal lesions with a maximum diameter less than 3 cm was performed by drawing a single ROI, whereas for those with a maximum diameter greater than 3 cm, three ROIs of the same size were used , taking care to avoid sampling necrotic, hemorrhagic, calcified and cystic areas.

Measurement of the mean and standard deviation (SD) of the ADC value of the other kidney was obtained by drawing a single ROI of the same size Positioned in correspondence with the site of the contralateral lesion.

Histopathological correlation

The final diagnosis was obtained from the pathological results of the surgical specimen in patients with operable masses. Correlation of the findings obtained using conventional, CE- MRI and DWI, including the image with b values of 0, 600 and 800s/mm2 with the results of the histopathological findings& follow up results was done for each patient.

2.6. Statistical analysis:

The collected data were computerized and statistically analyzed using SPSS program (Statistical Package for Social Science) version 24.0. Qualitative data were represented as frequencies and relative percentages. Chi square test was used to calculate difference between qualitative variables. Mann Whitney test was used to calculate difference between quantitative variables in not normally distributed data in two groups. Mann-Whitney U (MW test): was used for Comparing numerical variables between 2 groups, it is the non-parametric equivalent of t test, is used if the data cannot be assumed to have a normal distribution. Kruskal Wallis test (KW test): was used for Comparing numerical variables between more than 2 groups, it is the non-parametric equivalent of F test, is used if the data cannot be assumed to have a normal distribution.The results were considered statistically significant when the significant probability was less than 0.05 ($P < 0.05$). P-value < 0.001 was considered highly statistically significant (HS), and P-value ≥ 0.05 was considered statistically insignificant (NS).

3. Results:

the mean age of the studied patients was 54.07 ± 17.7 years old, with a range from 3 to 72 years old, more than ½ of the studied patients were male (56.7 %) **(Fig. 1).**About 3/4 of the studied renal masses were malignant (72.3%) and (26.7%) were benign **(Fig. 2).**

Clear cell RCC is the most common subtype in about third of cases 30%, followed by papillary RCC in 13.3%, angiomyolipoma and unclassified RCC were found in 10% of masses as illustrated in**Table (1).**

More than half of the studied masses were grade I and II (70% of Rcc) are classified into clinical low stage (grade I and II) and there is statistically difference between grades I, II and grades III, IV**(Table 2).**

Mean of the apparent diffusion coefficient (ADC) was

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significantly lower among malignant renal masses than benign masses, P-value < 0.05. **(Table 3).** As regard ROC curve for Cutoff of ADC mean, Area under the curve =0.5578, ADC > 1.85 (x10-3mm2/s) have sensitivity of 75 %, and specificity of 100 % with statistical significance in predicting benign renal mass **(Table 4, Fig. 3).**

There was statistically significant difference in mean of ADC in relation to different types of malignant RCC, mean of ADC was higher among Clear cell RCC and Willms tumor with no significant difference between them, while mean of ADC in Clear cell RCC was statistically higher than Papillary RCC, Chromophobe RCC and Unclassified RCC **(Table 5).**There was no statistically significant difference in mean of ADC in relation to different types of benign renal masses **(Table 6).**

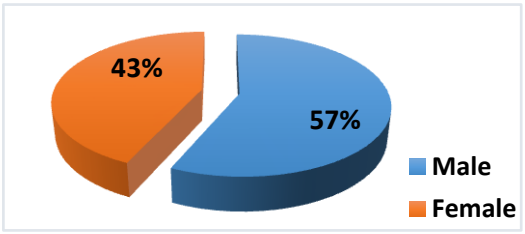


Figure (1): Pie diagram showing sex distribution among the studied patients (N=30).

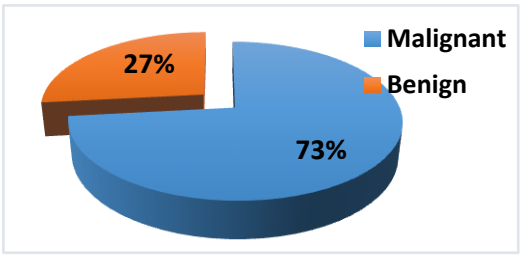


Figure (2): Pie diagram showing classification of the studied renal masses (N=30).

Table (2): Histopathological type of the studied renal masses

Histological type	Studied patients (N=30)	
	No.	%
Malignant tumor		
Clear cell RCC	9	30.0
Collecting duct RCC	1	3.3
Unclassified RCC	3	10.0
Transitional RCC	1	3.3
Chromophobe RCC	2	6.7
Papillary RCC	4	13.3
Willms tumor	2	6.7
Benign masses		
Abcess	1	3.3
Angiomyolipoma	3	10.0
Hemorrhagic cyst	2	6.7
Oncocytoma	1	3.3
Pyelonephritis	1	3.3

Table (3): Renal cell carcinoma grading and clinical stage.

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item	Studied renal masses (N=22)		ADC (x 10-3 mm2/S)
	No.	%	
grading of renal cell carcinoma			
I	9	45	1.72 ± 0.05
II	5	25	1.65 ± 0.17
III	4	20	1.23 ± 0.19
IV	3	15	1.1 ± 0.04

Table (4): The apparent diffusion coefficient (ADC) using Diffusion-weighted imaging in relation to classification of renal mass of the studied patients

ADC mean (x10-3mm2/s)	Benign renal masses (N=8)	Malignant renal masses (N=22)	Mann-Whitney test	p-value
Mean ± SD	1.77 ± 0.38	1.56 ± 0.24	38.000	0.018*
Median (Range)	1.9(1.12 - 2.1)	1.66(1.10 – 1.82)		(S)

Table (5): Cut off level of the apparent diffusion coefficient (ADC) using Diffusion-weighted imaging in relation to classification of renal masses with ROC curve:

Cutoff of ADC mean (x10-3mm2/s)	AUC	95%CI.	Sens.	Spec.	P-value
ADC mean> 1.85	0.784	0.522-1.00	75%	100%	0.019*

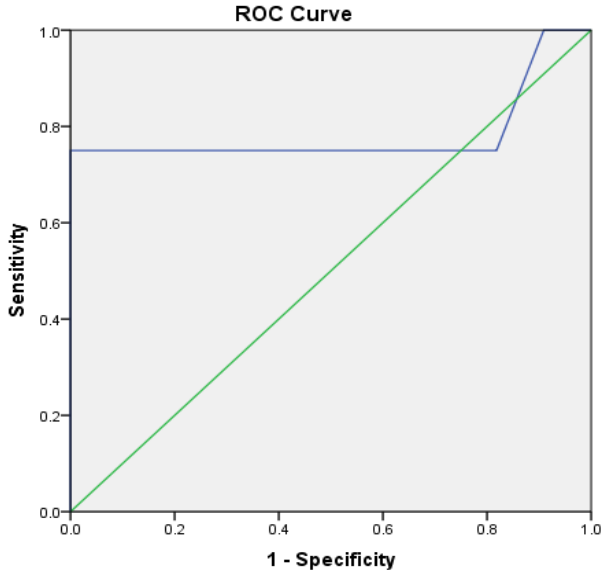


Figure 3: Cut off level of the apparent diffusion coefficient (ADC) using Diffusion-weighted imaging in relation to classification of renal masses

Table (6): The apparent diffusion coefficient (ADC) using Diffusion-weighted imaging in relation to type of malignant renal

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Mass

Malignant tumor	ADC (x10-3mm2/s)	Min-max	KWT	MWT
Clear cell RCC	1.74±0.05	1.67-1.82	0.005*	-----
Papillary RCC	1.62 ±0.02	1.6-1.65		0.003*
Chromophobe RCC	1.43 ± 0.014	1.42-1.44		0.036*
Collecting duct RCC	1.32 ± 0	1.32-1.32		2.000
Unclassified RCC	1.14 ± 0.04	1.11-1.20		0.009*
Willms tumor	1.77 ± 0.01	1.76-1.78		0.436
Transitional RCC	1.10 ± 0	1.10-1.10		2.000

Table (7): The apparent diffusion coefficient (ADC) using Diffusion-weighted imaging in relation to type of benign renal mass.

Benign tumor	ADC (x10-3mm2/s)	Min-max	KWT
Abscess	**1.12±0.0**	**1.12-1.12**	**0.179**
Angiomyolipoma	**1.93 ±0.05**	**1.88-1.98**	
Hemorrhagic cyst	**1.99 ± 0.01**	**1.98-2.0**	
Oncocytoma	**2.1 ± 0**	**2.1-2.1**	
Pyelonephritis	**1.2 ± 0.0**	**1.2-1.2**	

KWT: Kruskal Wallis Test
p-value> 0.05

4. Discussion:

Accurate assessment of renal masses is important for establishing whether tumors require surgical intervention or not **(1, 2)**. CT and MRI are the primary investigative tools for diagnosing, characterizing, and staging cystic or solid renalmass discovered incidentally by sonography. In many cases, the imaging tests still cannot easily differentiate benign from malignant lesions. Studies have shown that 16–33% of nephrectomies are performed on benign lesions **(6)**.

DW-MRI provides unique insight into tissue cellularity, tissue organization, integrity of cells and membranes, as well as the tortuosity of the extracellular space, which can be helpful for detecting malignant diseases, and for distinguishing tumor tissues from non-tumor tissues **(7)**.

The ADC has been related to the state of tissue during the growth of tumors or progression of cancer. With proliferating cells, there is an increase in cellular density and a decrease in the amount of intracellular space or extracellular space available, leading to a reduction in the ADC**(7)**.

In this study there is a statistically significant difference in the ADC value of malignant renal tumors compared to those of benign tumors.**Inci et al (8)** reported that Solid renal masses consist of predominantly enhancing tissue, may be either benign or malignant. Benign entities encountered in clinical practice include angiomyolipoma and oncocytoma. RCC is the most common malignant tumor of the kidney, but other entities such as transitional cell carcinoma and

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lymphoma may present as solitary solid primary renal masses. This is consistent with our study where renal cell carcinoma was the most commonly diagnosed renal lesion .It represented about 66.6% of all renal masses and about 90% of malignant renal masses. Angiomyolipoma represented 37.5% of benign studied renal masses and 10% of all examined renal masses.

Yoshikawa et al (9) also **Kilickesmez et al (10)**, found higher ADCs in AMLs than RCCs with the AML ADCs were gradually decreasing as the fat contents increased. AMLs with obvious fat content may be diagnosed easily using CT or conventional MRI. All the three studied cases in our study were of that type with obvious fat content.

We found that the ADC values for the cystic lesions are higher than those of the solid lesions and this agreed with **Zhang et al** .**(11)**

The mean ADC of RCC was also significantly lower than high ADC of hemorrhagic renal cyst **(1.99±0.01x10-3mm2/s).** This was in agreement with the previous reports by **Zhang et al. (11)**and **Inci et al. (8)**. However, **Yoshikawa et al. (9)**reported no significant difference between the ADC of RCC and the ADC of complex cysts.

In this study,the mean ADC value of benign hemorrhagic cyst was **(1.99±0.01x10-3 mm2/s)** , cystic RCC **(1.14±0.04 x10-3 mm2/s)**.this agreed with **El Hawary et al (12)** ,who reported the ADC values for benign cystic lesion significantly higher compared with the malignant cystic lesions **(3.35±0.3x10-3 mm2/s)** versus **(0.63±0.42x10-3 mm2/s)**

Taouli B. et al (13) calculated significantly lower ADCs in RCCs, indicative of restricted diffusion, than in simple cysts and oncocytomas. These results are similar to our findings of RCCs in which the mean of the measured ADC values of clear cell RCCs was **(1.74±0.05 x 10-3 mm2/s)** while it measured **(2.1 x10-3 x10-3 mm2/s)** in oncocytoma .

Accurate characterization of histological subtypes of RCC is important from prognostic and management perspectives.Clear cell RCC is the most common subtype (70%) that has aless favorable prognostic value than do papillary RCC(10%-15%)and chromophobe RCC (4%-6%). The management decision of renal tumors is tailored to histological subtypes. Moreover, patients with papillary or chromophobe RCCs have a higher 5-year survival rate than those with clear RCCs of the same stage. In this study ,the mean ADC value of clear type RCC was **(1.74±0.05x10-3 mm2/s)** , chromophobe RCC **(1.43±0.014 x10-3 mm2/s)**, papillary RCC **(1.62±0.02 x10-3 mm2/s)**. This agreed with **Manenti et al (14)** ,who reported significant difference among the ADC values of carcinomas and normal parenchyma In this work, the ADC value of clear and papillary subtypes is statistically different (P = 0.001) from other subtypes of RCC. This is attributed to the relatively larger extracellular spaces in the clear and papillary tumors compared to the other subtypes with subsequent unrestricted diffusion and relatively higher ADC values. **Zhang et al(11)**reported high ADC values for clear and papillary RCC **(2.03± 0.10 and 2.07± 0.17 x10-3 mm2/s)** respectively. **Taouli et al(13)** added that the papillary RCCs had lower ADCs than nonpapillary RCCs. On the other hand, **Sandrasegaran et al(15)** reported that there was insignificant difference in the ADCs of clear cell cancers and non clear cell cancers **(1.85 vs 1.97 x10-3 mm2/s; P = 0.18).** In addition,**Maneti et al(14)** added that there was no statistically significant difference between the ADC values of the different histologic types of

renal malignancy.

The ADC value for grade IV was the lowest **(1.1±0.04x10-3 mm2/s)** . There was a statistical significant difference between grades I **(1.72±0.05x10-3 mm2/s)** and II **(1.65 ±0.17x10-3 mm2/s)** and grades III **(1.23±0.19x x10-3 mm2/s) and and IV (1.1 ±0.04x10-3 mm2/s).**
This agreed with Studies by **Rosenkrantz et al**. **(16)**, and another study by **Yu, et al**. **(17)** concluded that the ADC value of low grade RCC (grades I and II) is significantly higher than that of high-grade RCC (grades III and IV).

5. Conclusion:

This work results demonstrate the potential utility of DW imaging for the characterization of renal masses. Most solid tumors showed restricted diffusion because of their higher cellularity, resulting in restriction of water movement and corresponding high signal intensity on DWI. The ADC value has been reported to be valuable for quantitatively distinguishing malignant from benign lesions with apparent diffusion coefficient.

6. ConflictofInterest: No conflictof interest.

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