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ROLE OF DIFFUSION WEIGHTED MRI AND ADC IN CHARACTERIZATION OF RENAL MASSES AND IN SUBTYPING OF RENAL NEOPLASMS.

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ABSTRACT

Early diagnosis of renal masses is essential for appropriate case management, differentiating benign from malignant renal masses and also identifying masses which need surgical intervention.Diffusion weighted MRI and ADC value helps in characterization of renal lesions. The mean ADC value of malignant lesions in our study [1.41 ± 0.17 x 10-3 mm2/s] was significantly lower than benign lesions [1.94 ± 0.32 x 10-3 mm2/s].ADC value of clear cell RCC [1.501 ± 0.03x 10-3 mm2/s] was significantly higher than that of Non clearcell RCC [1.152 ± 0.13 x 10-3 mm2/s].Thus,DW MRI and ADC values helps not only in pre-operative characterisation of the lesion into benign/malignant, but also in histological subtyping of renal neoplasms which has a role in prognosis and management.

KEYWORDS Diffusion weighted imaging, ADC, Renal cell carcinoma

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.[1,2]Early diagnosis of renal masses is essential for appropriate management, differentiating benign from malignant renal masses and also identifying masses which need surgical intervention.[3]

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. Application of diffusion-weighted sequences in body imaging had been limited. However, with 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.[4-6]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.[7-9] DW MRI can help in differentiating benign from malignant lesions and in subtyping of renal malignancies using ADC values.[10]The three most common subtypes of RCCs are clear cell, papillary, and chromophobe RCCs, accounting for 75%, 10–15%, and 5% of all RCCs, respectively. These subtypes have different histologic types, and clinical courses. Patients with chromophobe and papillary RCC show a better prognosis than do patients with clear cell RCC. Furthermore, these subtypes respond differentl to molecularly targeted therapies, particularly in patients with advanced and metastatic RCCs.Hence, it is important to identify the specific subtype of RCCs.

The purpose of our study was to evaluate role of Diffusion weighted MRI incharacterization of renal lesions and in differentiating the renal neoplasm into the varioussubtypes usingthe ADC values of the lesions.

MATERIAL AND METHODS

This prospective study was done in the Department of Radiodiagnosis&Krssna diagnostic centre of M.G.M. Medical College, Indore, Madhya Pradesh from March 2015 to August 2016 after getting approval by our Institutional Scientific Review Board. A total of 50 patients referred to our department with strong clinical suspicion of a renal lesion or having evidence of incidentally detected renal mass on ultrasound or CT scanwere subjected to MRI abdomen. The final study group comprised of 40 patients as some patients were excluded from the study because they lost follow up or lacked histopathology correlation.

MRI EQUIPMENT

MRI examination was performed on 3 TESLA, 97 CHANNEL MAGNETIC RESONANCE IMAGING equipment using a dedicated body coil for imaging the kidneys. MRI parameters are summarised in Table 1.The sequences used were Axial T1W, Axial T1W fat sat, Axial T2 W, Axial T 2W fat sat, Coronal T2W, DWI and 3 D LAVA.DWI was performed using respiratory gated 2D SPIN ECHO EPI sequence in the axial plane using b values of 0, 400and 800 sec/mm^2.

TABLE: 1 MRI scanning parameters

Image Plane	Acquisition scheme	TR/TE (ms)	Triggering	Slice Thickness (mm)	Fov(cm)	Matrix
Axial T1WI	Spoiled gradient echo	162 / 4.8	Breath hold	5	35 × 35	288x256
Axial T2WI	Singleshot Fastspin echo	5400 / 89	Breath hold	5	35 × 35	288x256
Coronal T2WI	Single shot fast spin echo	5400 / 89	Respiratory Triggered	5	35 × 35	288x256
DWI at b values 0,400,800	Spin echo single shot echoplanar	5100 / 61	Respiratory Triggered	5	35 x 35	128x128

Axial fat SatT1WI	Spoiled gradient echo	162 / 4.8	Breath hold	5	35 x 35	288x256
3D LAVA Axial T1WI	Spoiled gradient echo	4.4 / 2.1	Breath hold	4	40 x 40	320x160

IMAGE ANALYSIS

The Kidneys are viewed in T1W, T2W and DWI sequences with calculation of ADC values using the ADC maps. When multiple lesions are noted the most representative or largest of the lesion was taken into consideration.To measure the representative ADC of the renal lesion, circular Region of interest(area of 1 cm^2) were placed on the lesion in the areas showing restricted diffusion (visibly dark areas on ADC map). Care was taken to avoid necrotic or hemorrhagic areas within the renal lesion. For comparison of the ADCs of renal lesions, circular ROI of size approx. 1 cm^2 was placed on the normal renal parenchyma, without any preference for cortex /medulla. ADC values were expressed as Mean ± standarddeviation in the form of $10^{-3} mm^2/s$. A cut off ADC value of 1.55 x 10^{-3} mm^2/s is considered for differentiating benign from malignant lesions.

Follow up of all patients was done with surgery and histopathological correlation with biopsy or FNAC used as a reference standard. The final diagnosis was then made and results obtained are compared with Diffusion weighted imaging findings along with mean ADC values of the renal lesion.

Statistical analysis of data was done using SPSS software version.20 and the results were evaluated using Mann-whitney U test.

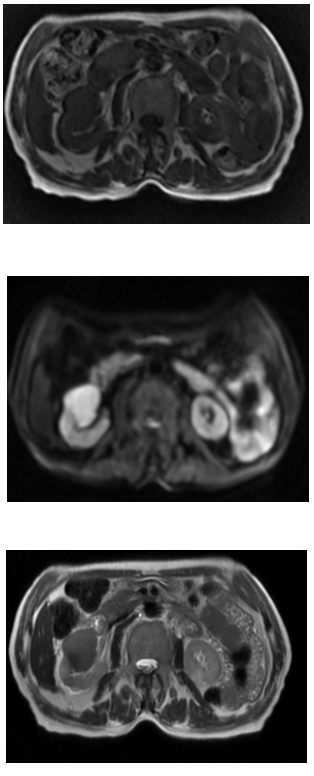
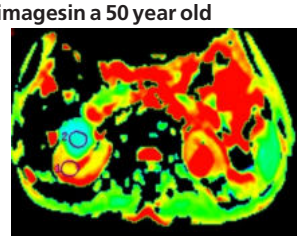


FIG: 1Axial MRI imagesin a 50 year old



male shows a lesionin right kidney which is hypointense On T 1 and T 2 WI (A and B), it shows restricted diffusion on DWI

C, ADC map (D) shows the ADC values of lesion (2) was 1.12 × 10^{-3} mm^2/secand uninvolved renalparenchyma(1)was 2.26 × 10^{-3} mm^2/sec. Diagnosis- Papillary RCC

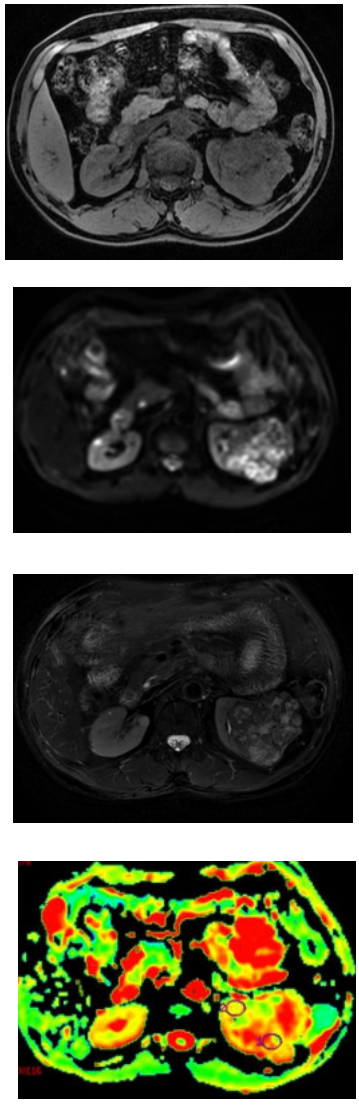


FIG: 2 Axial MRI images in a 65 year old male shows a lesion in left kidney which is Hypointenseon T 1 W images and heterogeneously hyperintense on T 2 W images.(A,B). It showsdiffusion restriction (C). ADC maps (D) showed the ADC value of lesion to be 1.44 × 10^{-3} mm2/sec (1) and uninvolved renal parenchyma(2) is 2.24 × 10^{-3} mm^2/sec. On follow up lesion was proved to be clear cell type RCC.

RESULTS

In our study most common age group of patients was 50-59 years (35%) with mean age of 50.7 years. The mean age of patients with benign lesions was 43.8 years and of patients with malignant lesions was 54.3 years. Majority of patients were males (26) constituting 65% of cases. On MRI, 8% (3) of renal lesions were classified as inflammatory 22% (9) lesions were benign and the remaining 70% (28) of renal lesions were classified as malignant lesions. Among the inflammatory lesions there were two cases (5%) of abscess and one of pyelonephritis which show significant diffusion restriction. The mean ADC value of abscess was 0.86 ± 0.3 ×10^{-3} mm^2 /sec and pyelonephritis was 1.56 ×10^{-3} mm^2/sec. Complex cysts (7%) had the highest ADC values of all benign

lesions with mean ADC values of 2.30 ± 0.3 × 10-3 mm^2 /sec. Angiomyolipoma was the most common benign lesion constituting 13% (5). Average ADC value of angiomyolipoma was 1.72 ± 0.2 ×10 -^{3} mm^2 /sec. Oncocytoma appeared as a well defined mass with a central cleft seen within the lesion. ADC value of oncocytoma was 1.84 ×10 -^{3}mm^2/sec. Malignant lesions of the kidney constituted 70% (28) of lesions of which renal cell carcinoma is the most common malignant neoplasm (63%). Clear cell RCC (18) is the most common histological subtype. Clear cell RCCs typically appear as expansile, cortical masses with areas of haemorrhage and necrosis.11Papillary RCC(4) demonstrates homogeneous low signal intensity on T2-weighted images as the tumour is hypovascular12. ChromophobeRCC(1) usually show cystic changes within a solid tumour.

25 RCCs were diagnosed on MRI, out of which majority of lesions were hypointense on T1 weighted, heterogeneous on T2 weighted images and most of them showed restricted diffusion on DW MRI. The mean ADC values of RCC in our study was 1.43 ± 0.2 ×10 -^{3} mm^2 /sec. Mean ADC value of clear cell carcinoma was 1.50× 10-^{3} mm^2/s, Papillary type ADC was 1.10× 10-^{3} mm^2/s and chromophobe type was 1.34× 10-^{3}mm^2/s. Two case of transitional cell carcinoma with mean ADC value of 1.40 ± 0.02 ×10 -^{3}mm^2 /sec which was slightly lower than that of RCC. The ADC value for renal metastasis was 0.95×10 -^{3}mm^2/sec.ADC value of normal renal parenchyma was 2.34 ± 0.3 x 10-3 mm2/s. The mean ADC value of malignant lesions in our study was 1.41 ± 0.17 x 10-^{3} mm^2/s and which was significantly lower than benign lesions [1.94 ± 0.32 x 10-^{3}mm^2/s] (p<0.05).

DISCUSSION

The present study showed that there is overlap in ADC values of inflammatory, benign and malignant lesions.When ADC values of RCC and Inflammatory mass lesions was compared inflammatory mass lesions had lower ADC than RCC. This can be attributed to the presence of thick viscous contents consisting of inflammatory cells, necrotic tissue and exudates[13]. Free diffusion usually corresponded to benign lesions while restricted diffusion could be seen in both benign and malignant lesions. Considering restricted diffusion as a marker for malignancy, we found high sensitivity (88%) and low specificity (36%). Hence nature of diffusion is a sensitive test for the detection of malignant lesions but not specific. Thus, DW MRI is used in conjunction with conventional sequences for accurate diagnosis of renal lesions.The mean ADC value of malignant lesions in our study [1.41 ± 0.17 x 10-^{3} mm^2/s] was significantly lower [14-15] than benign lesions [1.94 ± 0.32 x 10-^{3} mm^2/s]. Statistical analysis for ADC in differentiating benign and malignant groups with a threshold ADC value of 0.00155, had a sensitivity of 96%, specificity of 64% and p value<0.05.

We had a total of 23 RCCs in our study on follow up. This included 18 clear cell types (78.3%), 4 papillary (17.40%) and 1 chromophobe type of RCC (4.3%). These were clubbed as clear cell (78.3%) and non clear cell types (21.7%) for analysis. In our study the mean ADC value of clear cell RCC was highest among malignant lesions (1.501 ± 0.03 x 10-^{3} mm^2/s), ADC values for papillary RCC was 1.10 ×0.10 x 10-^{3}mm^2/s and for chromophobe type ADC value was 1.34 x 10-^{3} mm^2/s. Some studies16 have reported lower ADC values for papillary RCCs than that for non-papillary stating that this might be due to the fact that papillary and chromophobe RCCs are hypovascular lesions compared to clear cell RCCs and ADC values represent the combined effects of capillary perfusion and diffusion. There was no significant difference in the ADC values of papillary and chromophobe RCCs in our study.

In our study the mean ADC value of clear cell RCC [1.501 ± 0.03x 10-^{3} mm2/s] was significantly higher than that of non clear cell RCC [1.152 ± 0.13 x 10-^{3} mm^2/s]. Statistical analysis in differentiating clear cell and non clear cell types of RCC showed that for a threshold ADC value of 0.00145, sensitivity was 89%, specificity was 71% and p value <0.05 (Values above threshold indicated clear cell RCC).

The accurate identification of histological subtype of RCC is of clinical interest because of worse prognosis associated with clear cell carcinomas as compared to papillary and chromophobe carcinomas.Even in advanced disease, these subtypes are sensitive to different targeted immunotherapies like tyrosine kinase inhibitors sunitinib and sorafenib are effective against clear cell RCCs and rapamycin inhibitor temsirolimus is effective against papillary RCC[17-18].

We also evaluated role of DWI in differentiation of RCC with and without metastatic potential. In our study RCC with metastasis showed lower ADC value in comparison to RCC without metastasis [1.30 ± 0.2 vs 1.42 ± 0.30 (x 10-^{3} mm^2/s) though the difference was not statistically significant may be due to small sample taken in our study.

CONCLUSION

DW MRI and ADC values helps not only in pre-operative characterisation of the lesion into benign/malignant, but also in histological subtyping of renal neoplasms. It is imperative to establish a correct preoperative diagnosis to reduce the unnecessary surgeries for benign renal lesions, and also to avoid missing a malignant lesion.

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