Original Research Article

Diffusion MRI with quantification of ADC value in characterization of benign and malignant hepatic lesions and their correlation with cyto-histopathology

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ABSTRACT

Background: Diffusion weighted Imaging (DWI) is a useful noninvasive tool in MRI as it can be performed quickly and does not require contrast injection. In addition to it, DWI imaging and apparent diffusion coefficient (ADC) quantification not only can add additional anatomical data about the lesion but can also help in characterization of focal liver lesions into malignant or benign. The study attempts to establish a cut off value of ADC differentiating a benign from malignant lesion.

Materials and Methods : 32 patients with age group of 40-85 years with 46 diagnosed focal liver lesions on CT and MRI were included in the study. MRI was performed using 1.5 Tesla GE Healthcare HDxT machine. Conventional sequences followed by diffusion weighted sequences were acquired. Quantitative analysis was derived from ADC maps with calculation of ADC values. ADC values of the hepatic lesions were compared with histopathology as reference standard and analyzed statistically.

Results: In this study, 25 focal lesions in 18 patients had histopathological diagnosis of malignant pathology and had mean ADC value $1.13(x10^{(-3)}\text{mm}^2/\text{s})$ and 21 lesions in 14 patients with histopathological diagnosis of benign pathology had ADC value of $1.63(x10^{(-3)}\text{mm}^2/\text{s})$. Statistically significant difference between ADC value of benign and malignant lesions was found.

Conclusion: The study proclaimed that DWI with ADC quantification be used as an additional non invasive MRI tool to differentiate benign and malignant hepatic lesions with a sensitivity of 85.7%, specificity of 88%, PPV of 88% and NPV of 85.7%

1. Introduction

Conventionally, focal hepatic lesions are diagnosed and characterized on ultrasonography (USG) which is the first line of investigation because of easy availability and use of non ionizing radiation. Computed tomography (CT) is the next choice of investigation especially in suspected malignant lesions like HCC (hepatocellular carcinoma) which can add further information like enhancement pattern and multiplanar imaging.[1] The limitation with CT scan is the hazard of ionizing radiation associated with its use.[2]

Magnetic Resonance Imaging (MRI) can be used for further characterization as it has better contrast resolution and does not use ionizing radiations.[3,4] However in view of overlap in imaging finding of various lesions, further evaluation with histopathology is required. Biopsy of liver lesions is an invasive technique and can have serious complications.

Diffusion weighted Imaging(DWI) is a useful tool in MRI as it can be performed quickly and does not require contrast injection, in addition, DWI imaging and apparent diffusion coefficient(ADC) quantification can add to the anatomical data of MRI about the lesion like cellularity, cytotoxic edema etc.[5]

However, few other studies have reported that differentiation and characterization of focal lesions particularly solid benign lesion from malignant lesions such as focal nodular hyperplasia (FNH) from hepatocellular

carcinoma (HCC) on the basis of ADC value is not completely reliable as both can show overlapping result.[6–11]

In the absence of a reliable cut off value of ADC in differentiation of solid benign lesions from malignant lesions, this study aims to evaluate the role of diffusion weighted magnetic resonance imaging and quantification of ADC value in characterization of focal liver lesions and to determine a cut off value of ADC with cyto/histopathological correlation.

2. Materials and Methods

2.1. Data Extraction

The source of data were the patients with suspected or diagnosed focal liver lesions coming to the department of Radiodiagnosis, BLK Super speciality Hospital, Pusa road, New Delhi. The study duration was between June 2018 to May 2019. It was a prospective observational study where 46 focal hepatic lesions from 32 patients were studied that were detected on ultrasound or CT scan .Majority of the patients were in the age group of 40-70 years. Out of 46, 20 were male patients having 29 focal liver lesions and 12 were female patients having 17 focal liver lesions. Patients on pacemakers, prosthetic cardiac valves, claustrophobic patients or patients lost in follow up were not included in the study.

2.2. Method of evaluation

The approval of research protocol by the local ethics committee was taken and after taking informed consent from all the patients, they were explained about the procedure accordingly. The clinical details like history of present illness, past and family history were obtained.

All MR scans were performed on 1.5 T Signa HDxt Echospeed - GE Healthcare MR machine by using a standard body coil. Conventional MR sequences were acquired, firstly scout images were planned in all 3 orthogonal planes. Axial T1 weighted (W) spin echo; axial, sagittal and coronal T2 W fast spin echo (FSE); axial T1W, T2W fat sat (saturated)/ STIR(Short Tau Inversion Recovery), axial T1W contrast fat sat sequences were acquired. After acquiring the conventional sequences respiratory triggered single shot echo planar fat saturated diffusion weighted sequence in axial plane with tri directional diffusion gradients using b values of 0 and 800 s/mm^2 was acquired. Post processing was done on dedicated automatic advanced work station ADW4.4. ADC images were obtained from diffusion images using FUNCTOOL software at b value of 800m/s^2. Patients undergoing MRI for hepatic lesions were followed for their cyto-histopathology results and a correlation was drawn between the diffusion with ADC quantification and their cyto-histopathology diagnosis.

3. Results

Out of 32 patients included in the study, histopathology from the lesions seen on DWI confirmed 14 patients as having benign lesions (Figure 1) and 18 patients as having malignant lesions (Figure 2). The age and gender distribution of these results did not show any statistically significant difference (X2 = 0.847, p = 0.471). In totality, 56.3% patients had a malignant lesion (which included HCC and metastatic lesions as well). 43.8% patients had a benign lesion (which included a few inflammatory lesions and FNH)(Table 1) .
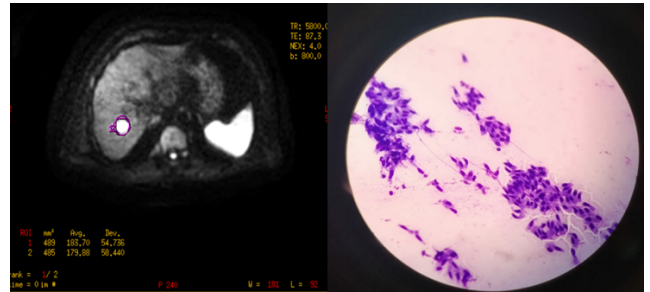

Fig. 1: DWI shows focal lesion in right lobe with diffusion restriction(right) and the corresponding histopathology from the lesion shows a benign etiology.
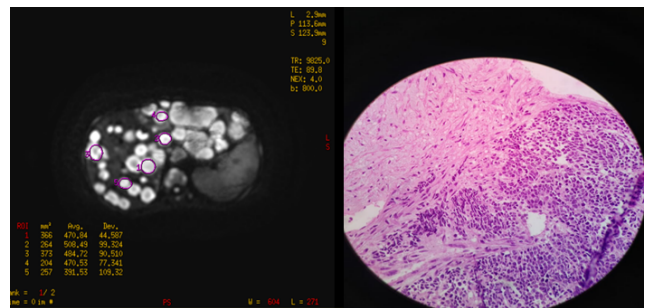

Fig. 2: DWI shows multiple lesions with restricted diffusion (right) and the corresponding histopathology from the lesions shows characteristics of malignant etiology.

The ADC value taken on the lesions seen on DWI (Figure 3) showed that the mean ADC Value in the histopathology proven malignant group was 1.13 (±0.22), and in the Benign group was 1.63 (±0.31). There was a significant difference in the two groups in terms of ADC Value (t = -6.576, p <0.001), with the ADC Value being significantly lower in the Malignant group.

The mean ADC Value in the HCC group was 1.05 (±0.2), in the CAGB Liver lesion group was 1.33 (±0.19), and in the Metastasis group was 1.2 (±0.1). There was a significant difference in the three groups in terms of ADC Value (H = 7.529, p = 0.023), with the ADC Value being significantly lower in the HCC group.

Table 1: Histopatholgy results in terms of different benign and malignant lesions and their relative percentages in the study group.

| Histopathologic Diagnosis	Number of patients	Number of focal liver lesions	Percentage
Benign	11	17	34.4%
Hepatocellular Carcinoma	10	15	31.3%
Liver Metastasis in Carcinoma Gall Bladder	6	7	18.8%
Metastasis from other abdominal organs	2	3	6.3%
Focal Nodular Hyperplasia	1	2	3.1%
Inflammatory Lesion	1	1	3.1%
Unsure	1	1	3.1%
Total	32	46	100.0%
Lesion	**Frequency**	**Percentage**	
Malignant	18	56.3%	
Benign	14	43.8%	
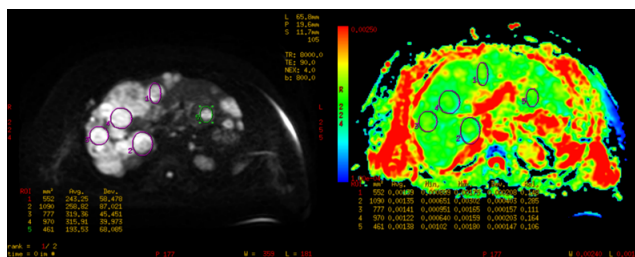
Fig. 3: DWI shows multiple lesions with restricted diffusion (right), corresponding ADC values were taken (left).

The receiver operating characteristic curve (ROC curve) depicting the diagnostic ability of ADC in predicting malignancy was drawn. Area under the curve was obtained as 0.910 with standard error of 0.043 (p value significant <0.001). At cutoff of 1.35, sensitivity of 88%, specificity of 88%, NPV of 88% and PPV of 85.7% was obtained (Table 2).
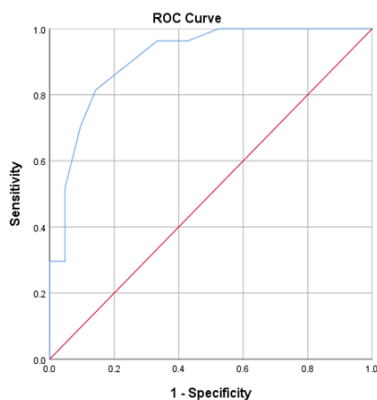
4. Discussion

Precise characterization of focal lesions into malignant or benign lesions can be a challenging task and is of utmost importance for proper treatment and follow up. MRI because of its increase spatial resolution and diagnostic capacity is done routinely for imaging of hepatic lesions. DWMRI has found an increasingly important role in characterization of focal liver lesions. Various studies in the past have stressed upon usefulness of ADC values in characterization of liver lesions but with significant difference of opinion.[6–15] In the present study no significant difference or bias was seen in various age groups or genders. Malignant lesions had a mean ADC of $1.13(x10^{(-3)}mm^2/s)$, while benign lesions had mean ADC value of $1.63(x10^{(-3)}mm^2/s)$. There was a significant difference between p value of benign and malignant lesions and can be inferred that using ADC values can reliably characterize focal lesions as benign or malignant with considerable accuracy. T. Ichikawa et al[12] evaluated 46 patients with 74 liver lesions. They suggested that significant difference between ADC values was seen in hemangiomas versus metastasis which is in coherence with our study in which metastatic lesions, HCC and benign lesions had significant difference between ADC value. Demir et al[14] in their study obtained mean ADC value$(x10^{(-3)}mm^2/s)$ for benign lesions as 2.5 and for malignant lesions as 0.86 thereby establishing that there is a significant difference in the mean ADC value and lesions could be characterised as benign or malignant on the basis of ADC values. Similar results were obtained by Miller et al,[6] who, in their study used b values of 0,500. Benign lesions had ADC value of 2.5 while malignant lesions had ADC value of 1.52.This difference was significant. Bruegel et al[15] used b values of 50,300,600 and obtained results with mean ADC value$(x10^{(-3)}mm^2/s)$ for normal liver parenchyma being 1.24 and value of 1.05 for metastasis and 1.22 for HCC. They found no significant difference in HCC and metastasis. This is contradictory to the findings of our study which suggests that there is a significant difference in the ADC value of HCC and metastasis. Overall 88% of lesions could be classified into benign and malignant taking 1.6 as a cut off similar to this study. The difference

Table 2: ROC curve showing discriminatory power of ADC value in predicting malignant lesions.

Area Under the Curve (AUROC)	Std Error	p value	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.910	0.043	<0.001	0.825	0.995
At Cut-Off = 1.35 (Smaller Value Represents Malignant Lesion)				
Sensitivity	Specificity	PPV	NPV	Diagnostic Accuracy
88.0%	85.7%	88.0%	85.7%	87.0%

in cutoff value could be attributed to different sets of b values being used. Young et al[16] in 2017 included 46 patients having 57 lesions in which they concluded that mean ADC value$(x10^{(-3)}mm^2/s)$ for benign solid focal lesions was 1.29 and 1.59 for malignant focal lesions. The calculated area under receiver operator curve for diagnosing a malignant liver lesion was 0.699 with a sensitivity of 96.9 and specificity of 52.0%, They found out unexpectedly high ADC value in some malignant focal lesions like one metastatic lesion. This is different from the results of our study in which all the metastasis and the malignant lesions had low ADC values.

Pankaj et al[17] obtained mean ADC value$(x10^{(-3)}mm^2/s)$ of malignant lesions as 1.09 and corresponding value of benign lesions as 1.67. All lesions above 1.8 were considered benign while below 0.95 were malignant. Cut off value thus obtained was 1.1 with sensitivity of 82 % and specificity of 86 % which corresponds to results obtained in this study.

Battal et al[18] conducted a study in 2011 in 143 focal liver lesions using a b value of 800 and his results were similar to our study, as in cutoff to differentiate benign from malignant lesions was 1.21 with specificity of 92% and diagnostic accuracy of 94%. Their study differed from the cutoff value of ADC of our study which could be attributed to the different machine settings and the different locations of various lesions.

5. Conclusion

The study proposed that DWMRI and ADC calculation with a cut off value 1.35 can be used as an adjunct to other MRI parameters for characterization of focal liver lesions into benign and malignant lesions with sensitivity of 85.7%, specificity of 88%, PPV of 88% and NPV of 85.7%. Its use in routine MRI evaluation of detected liver lesions can avoid unnecessary invasive procedures and can also help in better imaging workup and clinical outcome of the patients.

6. Acknowledgement

7. Source of Funding

8. Conflict of Interest

None.

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