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Original Research Paper

Radio-Diagnosis

DIAGNOSTIC UTILITY OF DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING AND APPARENT DIFFUSION COEFFICIENT VALUES IN THE EVALUATION OF FOCAL HEPATIC LESIONS: AN OBSERVATIONAL STUDY

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ABSTRACT **Background:** Diffusion-weighted magnetic resonance imaging (DW-MRI) has emerged as a valuable imaging modality in oncologic diagnostics by leveraging differences in the diffusion of water molecules across tissue compartments. Apparent diffusion coefficient (ADC) values derived from DW-MRI offer a quantitative approach to lesion characterization. **Objectives:** To evaluate the role of ADC values on DW-MRI in differentiating benign from malignant liver lesions and to assess their diagnostic performance in terms of sensitivity, specificity, and accuracy. **Materials And Methods:** This prospective observational study was conducted over 18 months at Sarvodaya Hospital and Research Centre, Faridabad, including 50 patients with hepatic lesions identified through imaging or biopsy. All participants underwent MRI with diffusion-weighted sequences on a 1.5T system. ADC values were quantitatively assessed for each lesion. Data were analyzed using standard statistical tests, and Receiver Operating Characteristic (ROC) analysis was performed to determine diagnostic performance. **Results:** The mean ADC value for malignant lesions was significantly lower ($0.738 \pm 0.051 \times 10^{-3}$ mm^2/s) compared to benign lesions ($1.98 \pm 1.163 \times 10^{-3}$ mm^2/s, $p < 0.001$). All malignant lesions exhibited hyperintensity on DWI and restricted diffusion. ROC analysis yielded an area under the curve (AUC) of 0.795, with an optimal ADC cut-off value of 1.085 $\times 10^{-3}$ mm^2/s, achieving 100% sensitivity, 75% specificity, and 92.0% overall diagnostic accuracy. **Conclusion:** ADC values obtained through DW-MRI offer a reliable, non-invasive imaging biomarker for differentiating benign from malignant liver lesions. Integration of ADC analysis into standard imaging protocols can enhance diagnostic accuracy, minimize unnecessary invasive procedures, and support clinical decision-making in the management of hepatic tumors.

KEYWORDS : Apparent diffusion coefficient, Diffusion-weighted MRI, Hepatic lesions, Liver tumors

INTRODUCTION

Diffusion-weighted magnetic resonance imaging (DW-MRI), established in the mid-1990s, has since evolved into a valuable tool for the assessment of various human disorders. This imaging technique relies on detecting variations in the mobility of water molecules across intracellular and intercellular spaces, providing insight into tissue microstructure.[1] Initially, DW-MRI gained clinical prominence through its rapid and accurate detection of acute ischemic stroke, often within seconds of onset.[2] Following its success in neurology, interest in DW-MRI expanded to include applications in oncologic imaging.[3]

Malignant tissues are characterized by altered cellular architecture, increased cellular density, and changes in the composition of the extracellular matrix when compared to normal tissue.[4] These differences restrict the diffusion of water molecules, producing measurable signal changes that can be captured using DW-MRI. Moreover, distinct tissue origins and tumor stages often exhibit unique diffusion patterns, making DW imaging a potentially powerful tool for lesion characterization.[5]

The liver is a common site for a wide spectrum of focal lesions, ranging from benign entities such as cysts, hemangiomas, and focal nodular hyperplasia to malignant tumors including hepatocellular carcinoma and metastases.[6,7] However, differentiating between these lesions using conventional imaging modalities can be challenging, especially in the presence of overlapping imaging features. While DW-MRI has shown promise in distinguishing benign from malignant hepatic lesions,[8] concerns remain regarding its sensitivity and specificity. Notably, there is no universally accepted cutoff for apparent diffusion coefficient (ADC) values—the quantitative parameter derived from DW-MRI—which limits its routine clinical application. Additionally, variability in technical parameters such as the selection of b-values across studies contributes to inconsistencies in imaging outcomes and diagnostic reliability.[9,10]

Despite its potential, the clinical utility of ADC values in differentiating hepatic lesions remains controversial due to the absence of standardized protocols and cutoff values. Furthermore, existing literature presents conflicting findings regarding optimal imaging parameters and diagnostic performance. Therefore, this study was conducted to evaluate the role of ADC values on diffusion-weighted MRI in differentiating benign from malignant liver lesions, and to assess their sensitivity, specificity, and predictive accuracy.

MATERIALS AND METHODS

This prospective observational study was conducted in the Department of Radiodiagnosis at Sarvodaya Hospital and Research Centre, Faridabad, Haryana, over a period of 18 months, from August 2022 to January 2024. Institutional Ethics Committee approval was obtained prior to study initiation, and written informed consent was obtained from all participants.

The study population included patients with focal liver lesions identified through imaging or biopsy. Patients aged 18 years or older were eligible for inclusion. Exclusion criteria comprised those with an unstable clinical condition, inability to cooperate during imaging (such as difficulty holding breath

or remaining still), claustrophobia, pregnancy, or the presence of metallic or electronic implants such as pacemakers, aneurysm clips, or cochlear implants.

A sample of 6 patients with benign and malignant hepatic lesions each was calculated using to assess the difference in mean ADC value between two groups. To measure difference of 0.368±0.213 in mean ADC values between the groups, a minimum of 6 patients per group was required to achieve a statistical power of 80% and a significance level (alpha) of 0.05. To increase power of the study, based on the inclusion and exclusion criteria, a total of 50 patients were enrolled and evaluated.[11]

Methodology

All participants underwent clinical examination followed by MRI, including diffusion-weighted imaging. The study utilized a 1.5T MAGNETOM ESSENZA MRI system to assess patients with focal hepatic lesions identified through ultrasound, CT, or biopsy. Patients fasted for at least four hours prior to scanning. DW-MRI was performed using a single-shot echo-planar imaging (EPI) sequence with diffusion gradients applied in three orthogonal directions. Images were acquired at b-values of 0, 400 and 800 s/mm. ADC maps were generated using all three b-values to facilitate quantitative analysis. ADC values were measured using dedicated post-processing software to aid in the differentiation between benign and malignant lesions.

Statistical Analysis

Data analysis was performed using Microsoft Office 365. Continuous variables were expressed as mean ± SD or median (IQR), and comparisons between groups were made using Student's t-test, Chi-square test, or Fisher's exact test as appropriate.[12] Receiver Operating Characteristic (ROC) analysis was used to determine the diagnostic performance of ADC values, with p-values <0.05 considered statistically significant.

RESULTS

The mean age of patients with benign tumors was 50.69±12.22 years, while that of patients with malignant tumors was 57.44±11.21 years. 43.8% of patients with benign tumors were female and 56.3% were male, compared to 44.1% female and 55.9% male in the malignant group. The differences in both mean age and gender distribution between the benign and malignant tumor groups were not statistically significant ($p>0.05$).

Among patients with benign liver tumors, the most commonly reported symptom was abdominal pain in 31.3%, fever in 25.0%, while vomiting, weight loss, loss of appetite, and discoloration in the eyes (jaundice) were not reported in any of the patients. In contrast, patients with malignant liver tumors, discoloration in the eyes (jaundice), loss of appetite, weight loss, were observed in all cases, pain in abdomen in 82.4% cases, vomiting in 70.6% of cases, and fever in 55.9% of cases.
On ultrasound, all benign lesions (100%) appeared well-circumscribed, compared to only 47.1% of malignant lesions. 56.3% of benign tumors appearing homogeneous, while all malignant tumors (100%) were heterogeneous. 56.3% of benign tumors were anechoic, and 31.3% were hyperechoic and rest 12.5% were isoechoic. In contrast, hypoechoic echotexture was predominant in malignant tumors (64.7%), while heterogeneous, hyperechoic, and isoechoic patterns were less common. Additionally, liver parenchymal disease was more frequently associated with malignancy (58.8%) than benign lesions (18.8%). The difference in ultrasonography findings between patients with benign and malignant tumors were statistically significant ($p<0.05$). [Table1]

In CT findings, all benign tumors appeared well-circumscribed, compared to 76.5% of malignant tumors. 56.2% of benign lesions were homogeneous, while all malignant lesions were heterogeneous. 87.5% in benign and 94.1% in malignant cases, appeared hypodense on non-contrast CT. However, contrast enhancement was seen in all malignant tumors and 43.8% of benign ones. Liver parenchymal changes were seen in 58.8% of malignant cases and 18.8% in benign ones. There was significant difference in CT-findings between benign and malignant tumour patients ($p<0.05$) except predominant density ($p>0.05$). [Table 2]

In MRI, On MRI, 50% of benign lesions and 61.8% of malignant lesions appearing as multiple lesions. All benign lesions were well circumscribed, whereas only 47.1% of malignant lesions had well-circumscribed borders. 43.8% of benign lesions were heterogeneous, and all malignant lesions were heterogeneous. Regarding the lobe of liver involved, there was no statistically significant difference ($p>0.05$). Liver parenchymal disease was more common in patients with malignant than benign tumors (58.8% vs 18.8%). On T1 weighted images, all benign lesions were hypointense, and in malignant tumor cases 82.4% were hypointense. On T2-weighted imaging, all lesions in both groups were hyperintense. The difference in MRI findings in margins, homogeneity, and liver parenchymal disease between benign and malignant patients were statistically significant ($p<0.05$). The mean ADC of the liver parenchyma was slightly lower in the malignant group ($1.18\pm0.09 \times 10^{-3}$ mm²/s) compared to the benign group ($1.20\pm0.05 \times 10^{-3}$ mm²/s), but this difference was not statistically significant ($p = 0.532$). [Table 3]

In DWI findings, 100% of malignant lesions, and 18.8% of benign lesions demonstrated hyperintensity. Restricted diffusion, was seen in all malignant tumors (100%), but only in 18.8% of benign tumors. This difference in both parameters was statistically significant ($p<0.05$). [Table 4]

The mean ADC value for benign lesions was $1.98 \pm 1.163 \times 10^{-3}$ mm²/s, signific antly higher than that of malignant lesions ($0.738\pm0.051 \times 10^{-3}$ mm²/s; $p<0.05$).

The diagnostic performance of ADC values in differentiating benign from malignant liver tumors was evaluated using ROC analysis. The area under the curve (AUC) was found to be 0.795 (CI- 0.605 to 0.985, SE- 0.097; $p<0.05$) indicating good diagnostic accuracy. An optimal ADC cut-off value of 1.085×10^{-3} mm²/s was identified as the threshold that best discriminates between benign and malignant liver lesions. In terms of diagnostic performance, the ADC cut-off value of 1.085 achieved a sensitivity of 100.0%, indicating that all malignant tumors were correctly identified. The specificity was 75.0%, reflecting a moderate rate of correctly identifying benign lesions. The positive predictive value (PPV) was 89.5%, and the negative predictive value (NPV) was 100.0%, meaning that a lesion with an ADC above the threshold is very unlikely to be malignant. The overall diagnostic accuracy was 92.0%, confirming that ADC is a highly effective, non-invasive imaging biomarker for differentiating benign from malignant liver lesions. [Figure 1]

DISCUSSION

This prospective observational study aimed to evaluate the diagnostic utility of ADC values obtained from diffusion-weighted MRI in differentiating benign from malignant liver lesions. DW-MRI is dependent on water's microscopic mobility. This mobility, which is attributed to thermal agitation and is largely controlled by the water's cellular environment, is known as Brownian motion. Therefore, results on DW-MRI may indicate a biologic issue before it's too late.[13]

In the present study, patients with malignant liver lesions had a higher mean age (57.44 ± 11.21 years) compared to those with benign lesions (50.69 ± 12.22 years), suggesting that

malignant lesions are more common in older individuals. Gender distribution was nearly equal in both groups, indicating no significant association with lesion type. These findings are consistent with those of Javadrashid et al[14], who reported a similar mean age for malignant cases (57.34±15.69 years). However, their benign group had a slightly lower mean age (46.14±34.21 years) and a higher proportion of female patients. The differences in gender distribution may reflect population-specific patterns, but overall, age appears to be a more consistent factor associated with malignancy.

Ultrasound and CT findings revealed that malignant tumors were more likely to exhibit heterogeneous echotexture, poorly defined margins, and liver parenchymal changes—findings consistent with prior radiologic observations. MRI findings, particularly in T1- and T2-weighted sequences, reinforced these differences, with malignant lesions demonstrating more frequent heterogeneity and association with parenchymal disease. In DW imaging specifically, hyperintensity and restricted diffusion were consistently observed in all malignant lesions but only occasionally in benign ones. This further validates DWI as a useful adjunct to conventional imaging in hepatic lesion evaluation.

In the present study, DWI and ADC values proved to be effective tools in distinguishing between benign and malignant liver lesions. The mean ADC value of malignant lesions was significantly lower ($0.738\pm0.051 \times10^{-3}$ mm²/s) than that of benign lesions ($1.98\pm1.16 \times10^{-3}$ mm²/s, $p<0.05$), reflecting the restricted diffusion typically associated with increased cellularity and reduced extracellular space in malignant tumors. Additionally, all malignant lesions showed hyperintensity on DWI with restricted diffusion, while only 18.8% of benign lesions displayed such characteristics ($p<0.05$).

The diagnostic performance of ADC values in differentiating benign from malignant liver tumors was evaluated using ROC analysis. The AUC was found to be 0.795 (CI: 0.605 to 0.985, SE: 0.097; $p < 0.05$), indicating good diagnostic accuracy. An optimal ADC cut-off value of 1.085×10^{-3} mm²/s was identified, which achieved a sensitivity of 100.0% accurately identifying all malignant lesions. The specificity was 75.0%, indicating a moderate ability to correctly classify benign lesions. The PPV was 89.5%, and NPV was 100.0%, suggesting that lesions with ADC above the threshold are highly unlikely to be malignant. The overall diagnostic accuracy was 92.0%, supporting ADC as a highly effective, non-invasive biomarker for hepatic lesion characterization.

Our findings are consistent with those of Youssef et al[11], who reported significantly lower ADC values for malignant liver lesions ($0.87\pm0.16 \times10^{-3}$ mm²/s) compared to benign lesions ($1.58\pm0.35 \times10^{-3}$ mm²/s, $p<0.05$). Their ROC analysis identified an optimal ADC cut-off of $\geq1.385 \times10^{-3}$ mm²/s with excellent diagnostic accuracy (AUC = 0.945), sensitivity of 100%, and specificity of 90.5%, comparable to our cut-off value of 1.085×10^{-3} mm²/s (AUC = 0.795), with 100% sensitivity and 75% specificity. This further supports the utility of ADC values as a diagnostic tool in hepatic lesion characterization.

Similarly, Elma Jahic et al[15] demonstrated statistically significant differences in mean ADC values between benign (1.88×10^{-3} mm²/s) and malignant (1.15×10^{-3} mm²/s) lesions, with an optimal cut-off of 1.341×10^{-3} mm²/s. The results align with our findings. Tarun Pankaj Jain et al[16] also reported a mean ADC of 1678 in benign lesions and 1097 in malignant lesions ($p<0.05$). An ADC threshold of 1260 provided 92% sensitivity and 80% specificity.

Additionally, Miller et al[17] reported a wide range of ADC values, with cysts and hemangiomas having the highest values and metastases among the lowest. They noted that using an ADC cut-off of 1.5×10^{-3} mm²/s yielded 57.1% sensitivity and 91.3% specificity, increasing to 63.5% and 86.4%, respectively, with a 1.6 cut-off. These thresholds are close to ours and suggest that optimal cut-off values may vary slightly depending on the imaging protocol and study population.

Overall, our findings, supported by multiple studies, underscore the high diagnostic value of ADC measurements in liver imaging. ADC provides a reliable, non-invasive, and reproducible method to differentiate benign from malignant hepatic lesions, with excellent sensitivity and good specificity. However, variability in ADC thresholds across studies suggests a need for standardized imaging protocols to enhance cross-institutional comparability and clinical implementation. The results demonstrated that ADC values serve as a reliable non-invasive imaging biomarker, with good diagnostic accuracy, high sensitivity, and reasonable specificity.

CONCLUSION

This study demonstrated that ADC values obtained through diffusion-weighted MRI serve as a valuable, non-invasive biomarker in the differentiation of benign and malignant liver lesions. All malignant lesions exhibited restricted diffusion and hyperintensity on DWI, with significantly lower mean ADC values compared to benign lesions. An ADC cut-off value of 1.085×10^{-3} mm²/s effectively distinguished malignant from benign lesions, with an overall diagnostic accuracy of 92.0%.

While conventional imaging features on ultrasound, CT, and MRI—including lesion margins, internal homogeneity, and associated liver parenchymal disease—showed significant differences between benign and malignant tumors, the addition of DWI and quantitative ADC mapping significantly enhanced diagnostic accuracy. In conclusion, integrating ADC evaluation into routine liver imaging protocols can significantly improve clinical decision-making, reduce the need for invasive procedures, and guide appropriate management strategies.

Table 1- Ultrasound findings in patients with benign and malignant tumors

Ultrasound		Benign		Malignant		p value
		Number	%	Number	%	
Well circumscribed	No	0	0.0%	18	52.9%	<0.001
	Yes	16	100.0%	16	47.1%	
Homogenous/ Heterogenous	Heterogenous	7	43.8%	34	100.0%	<0.001
	Homogeneous	9	56.2%	0	0.0%	
Predominant echogenicity	Anechoic	9	56.2%	0	0.0%	<0.001
	Heterogeneous	0	0.0%	4	11.8%	
	Hyperechoic	5	31.3%	6	17.6%	
	Hypoechoic	0	0.0%	22	64.7%	
	Isoechoic	2	12.5%	2	5.9%	
Liver parenchymal disease	No	13	81.2%	14	41.2%	0.014
	Yes	3	18.8%	20	58.8%	

Table 2- CT findings in patients with benign and malignant tumors

CT	Benign		Malignant		p value
	Number	%	Number	%	

Well circumscribed	No	0	0.0%	18	52.9%	<0.001
	Yes	16	100.0%	16	47.1%	
Homogenous/ Heterogenous	Heterogenous	7	43.8%	34	100.0%	<0.001
	Homogeneous	9	56.2%	0	0.0%	
Predominant density on NCCT	Hypodense	14	87.5%	32	94.1%	0.584
	Isodense	2	12.5%	2	5.9%	
Contrast enhancement	No	9	56.2%	0	0.0%	<0.001
	Yes	7	43.8%	34	100.0%	
Liver parenchymal disease	No	13	81.2%	14	41.2%	0.014
	Yes	3	18.8%	20	58.8%	

Table 3- MRI findings in patients with benign and malignant tumors

MRI		Benign		Malignant		p value
		Number	%	Number	%	
Number of lesions	Multiple	8	50.0%	21	61.8%	0.543
	Single	8	50.0%	13	38.2%	
Well circumscribed	No	0	0.0%	18	52.9%	**<0.001**
	Yes	16	100.0%	16	47.1%	
Homogenous/ Heterogenous	Heterogenous	7	43.8%	34	100.0%	**<0.001**
	Homogeneous	9	56.2%	0	0.0%	
Lobe of liver involved	Both	6	37.5%	15	44.1%	0.141
	Caudate	2	12.5%	0	0.0%	
	Left	1	6.2%	6	17.7%	
	Right	7	43.8%	13	38.2%	
Liver parenchymal disease	No	13	81.2%	14	41.2%	**0.014**
	Yes	3	18.8%	20	58.8%	
Predominantly on T1	Hypointense	16	100.0%	28	82.4%	0.159
	isointense	0	0.0%	6	17.6%	
Predominantly on T2	Hyperintense	16	100.0%	34	100.0%	-
	isointense	0	0.0%	0	0.0%	
ADC of liver parenchyma x1/1000 sq mm/s		1.20 ± 0.05		1.18±0.09		0.532

Table 4- DWI findings in patients with benign and malignant tumors

		Benign		Malignant		p value
		Number	%	Number	%	
DWI	Hyperintense	3	18.8%	34	100.0%	<0.001
	Hypointense	13	81.2%	0	0.0%	
DW Imaging: Restricted Diffusion/Non Restricted diffusion	No	13	81.2%	0	0.0%	<0.001
	Yes	3	18.8%	34	100.0%	
ADC of Liver Lesions		1.98 ± 1.163		0.738 ± 0.051		<0.001

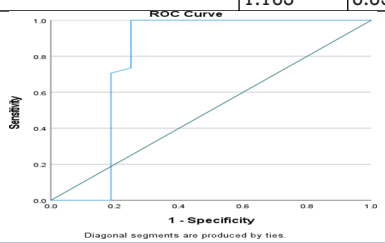

Figure 1- ROC curve for ADC as a Predictive Factor for malignancy in Liver Tumors

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