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Original Article

Radiology Section

Characterisation of Focal Liver Lesions using Diffusion-Weighted Magnetic Resonance Imaging Technique

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ABSTRACT

Introduction: Magnetic Resonance Imaging (MRI) is an important imaging modality for assessing and charactersing Focal Liver Lesions (FLLs). Diffusion-Weighted (DW) imaging, a powerful imaging tool, adds valuable information to MRI and provides unique information related to tumour cellularity and the integrity of the cellular membrane. The technique can be widely applied for tumour detection, tumour characterisation, and for monitoring the response to treatment.

Aim: To evaluate the role of Diffusion-Weighted Magnetic Resonance Imaging (DW-MRI) in differentiating between malignant and benign FLLs.

Materials and Methods: A total of 30 patients with FLLs diagnosed on Multi Detector Computed Tomography (MDCT) were evaluated. Demographic and clinical characteristics of all the patients were noted. Biochemical investigations, histopathological examinations, and radiological investigations, including Contrast-Enhanced Computed Tomography (CECT) imaging and DW-MRI were also performed and recorded. DW-MRI was performed with b values of 50, 400, and 800 mm^2/s; and Apparent Diffusion Coefficient (ADC) values were also calculated. SPSS 20.0 was used to analyse the data.

Results: Out of 30 FLLs diagnosed, 19 (hepatocellular carcinoma: 11 and metastatic FLLs: 8) were malignant and 11 (haemangiomas: 5, abscesses: 3, simple hepatic cysts: 2, focal nodular hyperplasia: 1) were benign. Among these, all the malignant lesions and three benign lesions, which showed typical imaging findings of abscess, displayed restricted diffusion. The cut-off mean ADC value: 1.077×10^{-3} sq. mm/sec was used to differentiate malignant and benign FLLs. The mean ADC value of benign FLLs was 1.372±0.308×10-3 sq. mm/s and mean ADC value of malignant lesions was $0.878\pm0.147\times10^{-3}$ sq. mm/s.

Conclusion: Overall, DW-MRI combined with ADC can be used to detect FLLs and serves as a diagnostic tool for differentiating them as malignant and benign.

Keywords: Contrast-enhanced multidetector computed tomography, Diagnostic tool, Diffusion-weighted imaging, Tumour detection

INTRODUCTION

MRI has emerged recently as a leading modality for evaluating and characterising FLLs/masses [1]. The use of faster sequences has permitted high-quality imaging of the whole liver with high inherent soft tissue contrast [2]. Diffusion-Weighted Imaging (DWI), a powerful MRI technique, is unique in providing information that reflects tumour cellularity and the integrity of the cellular membrane when compared to conventional techniques. The technique can be widely employed for tumour detection, tumour characterisation, and to monitor the treatment response [3].

DW-MRI technique derives its image contrast based on the differences in the mobility of protons (mainly associated with water) between the tissues [4-6]. The primary applications of DW-MRI include detecting early stages of acute cerebral stroke [7], demyelinating disease, and intracranial tumours [8-11]. DW-MRI measurements are rapid to perform (usually 1-5 min) and do not need the administration of exogenous contrast medium. Thus, DW-MRI can be appended along with the current imaging protocols without an increase in the examination time [3]. Moreover, due to substantial advancements in the hardware and coil systems, DW-MRI is appropriate for hepatic imaging with improved quality of image [12]. In addition, DW-MRI has the ability to prognosticate the response to chemotherapy and radiotherapy. Another recent development, the whole-body DW-MRI, has also reported substantial potential for tumour detection; however, it needs further evaluation [3].

DW-MRI is an attractive technique due to its assessment of tissue diffusivity without the use of gadolinium chelates and moreover the technique reduces the requirement of administering contrast medium during valuation of FLLs [12,13]. It is usually employed using two b values (e.g., $b=0$ s/mm^2 and $b=1000$ s/mm^2) to acquire meaningful interpretation [3]. ADC, a quantitative parameter calculated from DW-MRI, measures the diffusion in the biological system. It is useful in the differential diagnosis of malignant and benign hepatic lesions [13-15]. Reduction in mean ADC value postulates malignant lesions, while increased ADC values postulate benign lesions [16].

Further, the advent of parallel imaging techniques, particularly sensitivity encoding (SENSE), can be used to decrease the phase-encoding steps without the loss of spatial resolution [17,18]. This technique not only shortens the acquisition time and minimises echo-planar imaging artefacts, but also improves the quality of images acquired with DW single-shot echo-planar imaging [19]. Hence, the current study intended to evaluate the role of DW-MRI in differentiating between malignant and benign liver lesions based on ADC values.

MATERIALS AND METHODS

The present 1-year, hospital-based, cross-sectional study was conducted in the Department of Radiodiagnosis from January 2015 to December 2015. An ethical clearance was obtained from the Institutional Ethics Committee before the initiation of the study. Also, all the patients were briefed about the nature of the study and a written consent was taken from each participant. The study was conducted among 30 patients diagnosed for FLLs on contrast-enhanced MDCT of the abdomen. Exclusion criteria included postoperative patients, patients with hepatic neoplasms, who have undergone chemotherapy or radiation therapy, and patients with history of trauma. Patients with artificial pacemaker, metallic implants, and metallic foreign body were also omitted from the study.

Data Collection

Demographic characteristics of the study population including age and gender was recorded. The patients were then briefed about the procedure i.e., about the noise of the gradient coils and need to control the body movements for successful image acquisition. Along with this, biochemical investigations, radiological investigations (contrast-enhanced CT imaging and MRI), and histopathological examinations (of lesion sampled) were also performed.

Imaging Protocol

DW-MRI was conducted using Magnetom Symphony 1.5T MRI (Siemens, Germany) for imaging the patients diagnosed with FLLs. All the tests were performed using parameters, such as field of view (350-400 cm in adults; 180-200 cm in pediatrics), slice thickness (4-5 mm), and matrix size (512×512). DW-MRI was performed by following the steps sequentially: spin-echo T1 weighted (axial/ sagittal), spin-echo T2 weighted (axial/ coronal), and single shot echo-planar imaging (axial) with b-value of 50, 400,and 800 sec/ mm^2. The ADC values were calculated by marking three regions of interest and were correlated with results obtained on contrast-enhanced CT scan and histopathology or other laboratory investigations.

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS 20.0. The categorical data were expressed as rates, ratios, proportions, and percentages. The continuous data were expressed as mean±standard deviation. Chi-square test was used to compare the demographic and imaging features with ADC status. One-way ANOVA was used to compare MRI features with ADC scores. The p≤0.05 was considered statistically significant.

RESULTS

Based on the contrast-enhanced MDCT diagnosis, of the 30 patients with FLLs, 19 were malignant and 11 were benign. The demographic and clinical characteristics of the study patients are shown in [Table/Fig-1]. The patients were aged between 24 and 89 years with many patients in the age-group of 51-60 years. Majority (20%) of the patients presented with the chief complaint of jaundice and ascites. The mean alpha-fetoprotein level in patients with FLLs was 32.5 ng/mL.

Variable	n (%); n=30
Gender	
Male Female	19 (63.33%) 11 (36.67%)
Age (years)	
≤50 51-60 ≥61	7 (23.33%) 13 (43.33%) 10 (33.33%)
Clinical presentation	
Abdominal pain	3 (10%)
Ascites	6 (20%)
Fatigue	4 (13.33%)
Fever	1 (3.33%)
Jaundice	6 (20%)
Pain	2 (6.67%)
Upper gastrointestinal bleed	3 (10%)
None	5 (16.67%)
Mean alpha-fetoprotein level	32.5 ng/mL

[Table/Fig-1]: Demographic and clinical characteristics of the study patients.

The mean age of the patients was 56.7±13.53 years with a male to female ratio of 1.7:1. The mean duration of presenting complaints was 6.34 years; it was higher in patients with malignant FLL (6.89±4.14 years) than in patients with benign (5.37±3.77 years) FLL. However, the difference observed was not statistically significant (p >0.3236). The mean size of the malignant FLLs (6.21±3.43 cm) was larger than the benign FLLs (4.86±1.95 cm). However, the difference was not statistically significant (p>0.2443). Alpha-fetoprotein levels were significantly raised in patients diagnosed with malignant FLLs (47.86±35.70 ng/ml) when compared to benign FLLs (6.18±3.43 ng/ml; p=0.0007).

The comparison of CECT features, presence of necrosis, type of lesions, MRI features, biopsy status, and FLL subtypes along with ADC status are summarised in [Table/Fig-2]. Of total 19 patients with malignant FLLs, 10 patients showed hyperintense arterial phase. Whereas, 18 out of the 19 lesions showed washout of contrast on delayed phase and appeared isointense or hypointense. Among the patients with malignant lesions, only four of them showed portal vein invasion. Necrosis was observed in eight and two of

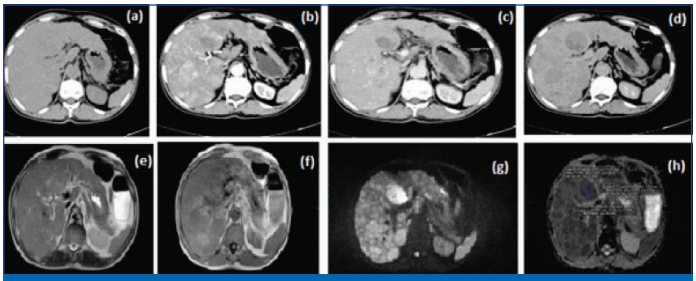
Variable		ADC status		p-value
		Malignant, n (%)	Benign, n (%)	
Age (years)	≤50 51-60 ≥61	2 (28.57) 9 (69.23) 8 (80.00)	5 (71.43) 4 (30.77) 2 (20.00)	0.0807
Gender	Male	14 (73.68)	5 (26.32)	0.1221
	Female	5 (45.45)	6 (54.55)	
CECT Features	**NECT** Hyperintense Hypointense Isointense Isointense/Hypointense	 0 15 (68.18) 2 (100.0) 2 (40.0)	 1 (100.0) 7 (31.82) 0 3 (60.0)	0.360
	Arterial phase Hyperintense Hypointense Isointense Isointense/Hypointense	 10 (83.33) 0 0 9 (75)	 2 (16.67) 5 (100) 1 (100) 3 (25)	0.0010*
	Venous phase Hyperintense Hypointense Peri Enhancement	 8 (80.0) 3 (33.33) 8 (72.73)	 2 (20.0) 6 (66.67) 3 (27.27)	0.0780
	Delayed phase Hyperintense Hypointense Isointense Isointense/Hypointense	 1 (50.0) 8 (57.14) 8 (80.0) 2 (50.0)	 1 (50.0) 6 (42.86) 2 (20.0) 2 (50.0)	0.3970
	Portal vein invasion Yes No	 4 (100.0) 15 (57.69)	 0 11 (42.31)	0.2810
Necrosis	Yes No	8 (80.0) 11 (55.0)	2 (20.0) 9 (45.0)	0.3481
Types of lesions	Single Multiple	6 (50.0) 13 (72.22)	6 (50.0) 5 (27.78)	0.3950
MRI Features	**T1WI** Hypointense Isointense Isointense/Hypointense	 17 (68.0) 1 (33.33) 1 (50.0)	 8 (32.0) 2 (66.67) 1 (50.0)	0.4611
	T2WI Hyperintense Isointense Isointense/Hypointense	 19 (67.86) 0 0	 9 (32.14) 1 (100.0) 1 (100.0)	0.7781
	Restricted diffusion Yes No	 19 (86.36) 0	 3 (13.64) 8 (100.0)	0.0060*
Biopsy	Yes No	11 (84.62) 8 (47.06)	2 (15.38) 9 (52.94)	0.0830
FLL subtypes	Haemangioma Abscess Cyst Focal nodular hyperplasia Hepatocellular carcinoma Metastases	0 0 0 0 11 (100.0) 8 (100.0)	5 (100.0) 3 (100.0) 2 (100.0) 1 (100.0) 0 0	-

[Table/Fig-2]: Comparison of demographic, contrast enhanced computed tomography features, magnetic resonance imaging features with apparent diffusion coefficient status (malignant and benign).
ADC: Apparent diffusion coefficient; CECT: Contrast-enhanced computed tomography; NECT: Non-enhanced computed tomography; FLL: Focal Liver Lesions; MRI: Magnetic resonance imaging; WI: Weighed image; p-values indicate comparison of all the mentioned features with ADC status (malignant and benign lesions); *Statistically significant

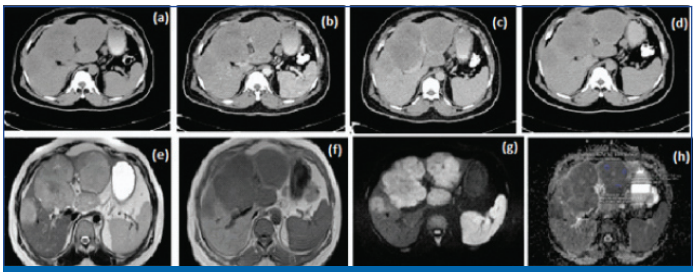
the malignant and benign lesions, respectively. All the malignant cases showed restricted diffusion, whereas only three benign cases showed restricted diffusion, which were cases of hepatic abscess. The difference observed was statistically significant (p=0.006). Out of 30 samples, 13 were biopsied, among which 11 were malignant lesions and two were benign i.e., abscess.

The most common malignant lesion was hepatocellular carcinoma (36.67%), while the most common benign lesion was haemangioma (16.67%).The lesions were characterised as malignant and benign according to the CT and DW-MRI imaging [Table/Fig-3-8]. CT reveals multiple well-defined lesions involving both the lobes of the liver, which show early enhancement on arterial phase with washout on venous and delayed phases. DW-MRI shows multiple hyperintense lesions, which show restricted diffusion with a mean ADC value of 0.720×10^{-3} sq. mm/s [Table/Fig-3]. Limited MRI reveals multiple T2 hyper intense lesions involving both the lobes of the liver; DW-MRI reveals restricted diffusion in these lesions with a mean ADC value of 0.708×10^{-3} sq. mm/s [Table/Fig-4]. DW-MRI shows lesions without restricted diffusion with a mean ADC value of 1.644×10^{-3} sq. mm/s [Table/Fig-5]. DW-MRI shows lesion with restricted diffusion with an ADC value of 0.790×10^{-3} sq. mm/s [Table/Fig-6]. DW-MRI shows the cyst without restricted diffusion with a mean ADC value of 2.176×10^{-3} sq. mm/s [Table/Fig-7]. DW-MRI shows ADC value map without restricted diffusion with an ADC value of 1.056×10^{-3} sq. mm/s [Table/Fig-8].

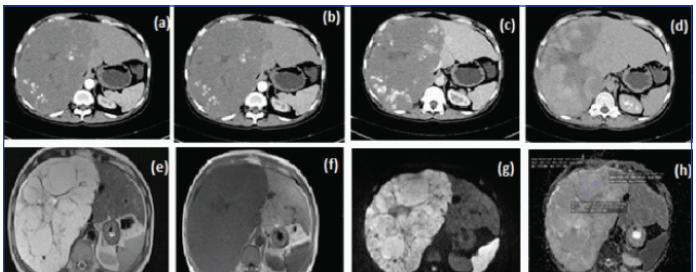
There was a statistically significant difference between mean ADC values and restricted diffusion, biopsied samples, and FLL subtypes ($p<0.01$) [Table/Fig-9].



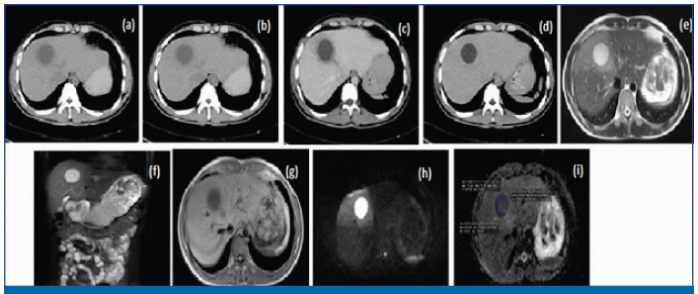
[Table/Fig-3]: A 60-year-old male patient with multicentric hepatocellular carcinoma: (a) CT-plain; (b) CECT arterial phase; (c) CECT venous phase; (d) Delayed phase; (e) MRI axial T2WI; (f) MRI axial T1WI; (g) DW-MRI, b 800; (h) ADC map.



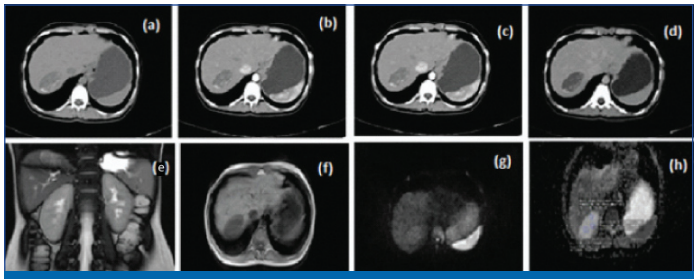
[Table/Fig-4]: Multiple biopsy showing adenocarcinoma liver metastases from unknown primary adenocarcinoma liver metastases: (a) CT-plain; (b) CECT arterial phase; (c) CECT venous phase; (d) Delayed phase; (e) MRI axial T2 WI; (f) MRI axial T1WI; (g) DW-MRI, b 800; (h) ADC map.



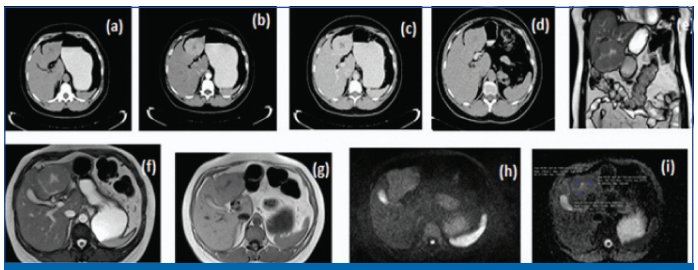
[Table/Fig-5]: Giant haemangiomas showing periphery puddling on contrast study characteristic of haemangiomas: (a) CT-plain; (b) CECT arterial phase; (c) CECT venous phase; (d) Delayed phase; (e) MRI axial T2WI; (f) MRI coronal T1WI; (g) DW-MRI, b 800; (h) ADC map.



[Table/Fig-6]: A 27-year-old male patient with a lesion with characteristic imaging feature of hepatic abscess: (a) CT-plain; (b) CECT arterial phase; (c) CECT venous phase; (d) Delayed phase; (e) MRI axial T2WI; (f) MRI coronal T2 WI; (g) MRI axial T1WI; (h) DW-MRI, b 800; (i) ADC map.



[Table/Fig-7]: A well-defined non-enhancing lesion with few tiny specks of calcification in segment 7 suggestive of hepatic cyst: (a) CT-plain; (b) CECT arterial phase; (c) CECT venous phase; (d) Delayed phase; (e) MRI coronal T1WI; (f) MRI axial T2 WI; (g) DW-MRI, b 800; (h) ADC map.



[Table/Fig-8]: A 40-year-old female patient with a focal nodular hyperplasia, with a central scar in segment: (a) CT-plain; (b) CECT arterial phase; (c) CECT venous phase; (d) Delayed phase; (e) MRI coronal T2 WI; (f) MRI axial T2WI; (g) MRI axial T1WI; (h) DW-MRI, b 800; (i) ADC map.

Variable	Groups	ADC values (Mean±SD)	p-value
T1WI	Hypointense	1062.83±430.52	0.8755
	Isointense/Hypointense	1085.15±190.00	
	Isointense	1195.83±397.35	
T2WI	Hyperintense	1073.32±422.80	-
	Isointense/Hyperintense	1219.50±0.00	
	Isointense/Hypointense	1056.00±0.00	
Restricted diffusion	Yes	882.49±141.64	0.0001*
	No	1414.65±501.37	
Biopsy	Yes	865.28±156.36	0.0102*
	No	1239.99±468.98	
FLL subtypes	Abscess	857.93±59.52	0.0001*
	Cyst	1891.65±402.84	
	Hepatocellular carcinoma	868.35±168.63	
	Haemangioma	1650.90±316	
	Metastases	888.64±127.19	
	Focal nodular hyperplasia	1056±0.00	

[Table/Fig-9]: Comparison of magnetic resonance imaging features with mean apparent diffusion coefficient values.
ADC: Apparent diffusion coefficient values; FLL: Focal liver lesions; WI: Weighed image; *Statistically significant

The best threshold mean ADC value was 1.077×10^{-3} sq. mm/sec for differentiation between malignant and benign FLLs. Hence, the mean ADC value of the 11 benign lesions was $1.372\pm0.308\times10^{-3}$

sq. mm/s. While, mean ADC value of the 19 malignant lesions was 0.878±0.147×10^{-3} sq.mm/s [Table/Fig-10].

Final Diagnosis	Mean ADC (x10^{-3} sq. mm/s)±SD
Malignant lesions	
Hepatocellular carcinoma (n=11)	0.868±0.168
Metastasis (n=8)	0.888±0.127
Mean ADC for malignant lesions (n=19)	0.878±0.147
Benign lesions	
Haemangioma (n=5)	1.650±0.316
Abscess (n=3)	0.857±0.059
Simple cyst (n=2)	1.891±0.402
Focal nodular hyperplasia (n=1)	1.056±0.000
Mean ADC for benign lesions (n=11)	1.372±0.308
Grand total	1.077±0.408

[Table/Fig-10]: Mean apparent diffusion coefficient values of focal liver lesion subtypes.
ADC: Apparent diffusion coefficient

DISCUSSION

Dynamic contrast examination, which requires contrast material to enhance the quality of images is expensive and carries potential side-effects, whereas DW-MRI can be used without any necessity for contrast material, within the duration of held breath [20]. In addition, early detection and characterisation of the FLLs are challenging for the radiologists. During the past two decades, the advancement in MRI scanners and fast imaging MRI techniques enabled the accurate characterisation of FLLs. Although, several studies have suggested the importance of DW-MRI and ADC in the differentiation of malignant and benign lesions, still it remains uncertain; for instance, vascular metastasis is often confused with haemangiomas during imaging [12]. Thus, the current study focused to evaluate the role of DW-MRI in differentiating between malignant and benign liver lesions.

The current study emphasised the diagnostic accuracy of DW-MRI to distinguish malignant and benign FLLs, which is similar to that noted in various other studies [4,12]. Specific cut-off ADC value was used in this study to distinguish between malignant and benign FLLs as done in previous reports [1,21]. In our study, 1.077×10^{-3} sq. mm/sec was considered as the mean threshold or cut-off value to differentiate malignant and benign FLLs. The mean ADC value for benign focal hepatic lesion in this study was similar to study published by Bruegel M et al., [22]. In case of malignant FLLs, the mean ADC value is comparable to that of other studies [4,12].

In our study, to differentiate between malignant and benign hepatic lesions using DW-MRI, we evaluated the signal intensity changes using a b-value of 50 s/mm^2, 400 s/mm^2 and 800 s/mm^2. Although, suboptimal signal-to-noise ratio and artifacts hinder the detection of the FLLs, a high b-value DW-MRI facilitates the differentiation of malignant FLLs from haemangioma and cysts. Malignant lesions showed high signal intensity due to restricted diffusion of extracellular water molecules whereas cystic lesions, such as haemangiomas and cysts exhibited decreased signal intensity at increasing b-values owing to a high fluid content. However, some haemangiomas showed perseverance of high signal in some part of the lesion.

Theoretically, ADC values are obtained using two different b-values. In addition, ADC values depend upon the types and quantities of b-values as well as diffusion of tissues. Also, it is stated that, ADC values are accurate if the b-values are higher [23]. Likewise in our study, malignant lesions showed high signal attenuation on DW-MRI using a high b-value (800 sec/sq. mm) rather than a b-value of 50 sec/sq. mm. Conversely, benign lesions, including haemangiomas and cysts showed low signal intensity on DW-MRI using a high b-value (800 sec/sq. mm) than at b-value of 50 sec/sq. mm. The malignant FLLs showed true restriction of diffusion on DW-MRI and ADC map. Whereas, benign lesions showed absence of restricted diffusion on DW-MRI and ADC map. Therefore, out of 30 patients with FLLs studied, 27 FLLs were differentiated into malignant and benign lesions by visual assessment with DW-MRI and ADC value. However, the other three cases could not be differentiated as they were the cases of abscess.

Benign lesions, such as liver cysts and haemangiomas showed higher ADC values than malignant lesions, such as hepatocellular carcinomas and metastases. Concurrent to our findings, several studies have reported significantly higher ADC values in benign compared to malignant FLLs [24,25]. Sometimes ADC values are often variable among various studies, which is partly related to different equipment and different b-values. To sense smaller diffusion distances and slow-moving water molecules, b-values should be higher. However, if the b-values are smaller, ADC value tends to be larger, because of reduction in signal strength due to diffusion and contamination of ADC values by micro-perfusion [26].

LIMITATION

The potential limitations encountered in the study include the following: hepatic abscess cases that showed restricted diffusion in our study had lower ADC values. The diagnosis in these cases relied upon clinical and CECT findings. Despite there being significant differences in mean ADC values of malignant and benign FLLs on a group basis, characterisation of FLLs using ADC values showed overlap in the present study. Another limitation of our study was that only few individuals with FLLs were studied when subgroups were taken into consideration; for example, benign hepatocellular lesions, such as hepatic adenoma were not observed in our study. Hence, comparison was not conducted between solid malignant and benign masses.

CONCLUSION

Malignant FLLs show true restriction of diffusion on DW-MRI and have low ADC value than that of benign FLLs. Hence, DW-MRI combined with ADC can be used as a screening tool for detecting FLLs and as a diagnostic tool for characterising them as malignant or benign. DW-MRI must be done both at low and high b values for high sensitivity for the detection of FLLs. The DW-MRI sequence is a useful diagnostic tool, since it can be performed in free breathing; there is no need to use contrast media, and it can accurately diagnose and differentiate malignant and benign hepatic masses. However, studies on variants of FLLs are required for evaluation of DW-MRI in characterisation of hepatic masses.

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