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Original Article

Qualitative and quantitative magnetic resonance imaging assessment of focal liver lesions: a study to evaluate the role of different MRI sequences

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Abstract

Introduction: Focal liver lesions have broad differential diagnoses. With its improved soft tissue characterization and newer sequences, magnetic resonance imaging (MRI) can significantly narrow the differential diagnoses, especially when discriminating benign from malignant lesions.

Methods: T1, T1 in-phase and out-of-phase, T2, long TE T2, and diffusion-weighted imaging (DWI) were performed in 159 patients with ultrasound documented focal liver lesion. Qualitative and quantitative assessment of apparent diffusion coefficient (ADC) values and long TE images were done, and a threshold for differentiating benign from malignant lesions was obtained. The MRI diagnosis was compared with the final diagnosis obtained from histopathology in most cases or the follow-up, and other tests (markers and RBC scan) where histopathology was not available. Sensitivity, specificity, and accuracy of MRI sequences in differentiating various focal lesions were obtained.

Results: T1 weighted images were useful for identifying fat, hemorrhage, and iron within the lesions. T2 weighted imaging was able to correctly classify 82.0% of the malignant lesions and 83.7% of the benign lesions. Long TE T2 images were highly accurate in distinguishing haemangiomas and cysts from solid lesions. On DWI, 89.5% (i.e., 60 out of 67) of the lesions were correctly classified as malignant, and 88.0% (i.e., 81 out of 92) of the lesions were correctly classified as benign. Threshold ADC value of 1.37×10^{-3} mm^2/s is highly accurate for differentiating malignant from benign lesions.

Conclusion: DWI is a sine qua non in liver lesion assessment allowing improved detection and characterization. Long TE T2 weighted imaging can accurately detect haemangiomas and cysts, and rule out metastasis.

Introduction

The term focal liver lesion includes a broad spectrum, ranging from benign cysts to highly malignant hepatocellular carcinoma and metastases. Accurate detection and characterization of focal liver lesions are paramount for appropriate treatment in a wide variety of clinical settings.[1] Correct identification of benign lesions (e.g., hemangiomas) will prevent unnecessary invasive procedures. Detection, characterization, enumeration, and localization of primary or metastatic hepatic neoplasms are critical for planning appropriate therapy.

The optimal imaging modality for detecting and characterizing focal liver lesions has been robustly debated over the past two decades. Imaging modalities currently available to specifically evaluate focal liver disease include trans-abdominal and intra-operative ultrasound, triphasic computed tomography (CT), computed tomographic arterial portography (CTAP), and magnetic resonance imaging (MRI) enhanced with one or more types of contrast agent. These are often complementary, and various combinations may be appropriate in different clinical settings. Most would now agree that MRI with contrast has surpassed all of these modalities in terms of lesion characterization, or is at least equal to each one in detection. This is due to the high intrinsic soft-tissue contrast, improved biochemical and anatomic information, sensitivity to perfusion differences, multi-planar capability, and lack of ionizing radiation.[2] The general consensus of evidence suggests that dynamic gadolinium-enhanced imaging alone is the best technique for the detection and characterization of focal liver lesions.[3-7] The goal of a complete, non-invasive evaluation of the liver has been realized and is widely available with modern scanners and techniques. For focal liver lesion detection and characterization, MRI relies on T1-weighted, T2-weighted, diffusion-weighted

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imaging (DWI), and dynamic gadolinium-enhanced T1-weighted imaging.[8,9] DWI can characterize lesions based on their ADC values without the need of T1 and T2 relaxation times or contrast administration. Differences in cellularity between benign and malignant liver lesions resulting in different diffusion properties of water protons within these lesions are reflected by different apparent diffusion coefficient (ADC) values measured by DWI.[10] Several studies have identified significantly lower ADC values in malignant lesions compared to benign focal liver lesions.[10-12] Hepatic abscesses show extremely low ADC values in most cases due to viscous contents and are therefore an exception to this rule.[13,14] However, the differentiation of benign solid lesions like focal nodular hyperplasia (FNH) and adenoma from malignant lesions is often difficult by DWI, as there is considerable overlap of ADC values between both groups.

Long TE T2 weighted images have recently been used to differentiate haemangiomas and cysts from solid malignant lesions. The mean T2 relaxation times of cysts, haemangiomas, and malignant tumors are 341 ± 38 msec, 142 ± 40 msec, and 76 ± 11 msec, respectively, with a cutoff T2 value of 112 msec that discriminates hemangiomas and malignant tumors.[15]

Our study aimed to evaluate the role of various MRI sequences in discriminating various focal liver lesions and build a comprehensive protocol for assessing these lesions using MRI. We also aimed to evaluate the role of DWI and Long TE T2 weighted images in discriminating benign and malignant hepatic lesions.

Methods

This study was a prospective observational one, conducted in the Department of Radio-Diagnosis and Imaging at Sher-i-Kashmir Institute of Medical Sciences, Srinagar, after taking due clearance from the institutional ethical committee (IEC). In all cases informed consent was obtained from the patient or his/her attendant. We included patients with ultrasonography (USG) documented focal liver lesion(s) in our study, irrespective of age and sex. Patients with history of contrast hypersensitivity, pregnant females and those with deranged renal functions were excluded.

Examination techniques and imaging protocols

All magnetic resonance (MR) studies were performed using 1.5 tesla magnetic resonance system (Magnetom Avanto, Siemens Medical System). After the preliminary localizing sequence, the imaging protocol included:

1. Trans-axial breath-hold T1-weighted fast low angle shot (FLASH) 2D in and out of phase (TR/TE 100/2.22; flip angle 70°; section thickness 6 mm).
2. Trans-axial breath-hold T1-weighted FLASH 2D with and without fat suppression (TR/TE 221/7.15; section thickness 6 mm).
3. Trans-axial breath-hold T2-weighted turbo spin-echo (TSE) with and without fat suppression (TR/TE 4000/103; section thickness 6 mm).
4. Trans-axial breath-hold T2-weighted TSE with increasing TE values (78, 171 and 279 ms).
5. Respiratory-triggered diffusion-weighted sequence was performed using three b-values (b=50 s/mm^2, b=400 s/mm^2, and b=800 s/mm^2). The quantitative analysis of diffusion (i.e. ADC) was calculated on a picture archiving and communication system (PACS) workstation by applying a region of interest (ROI) on the image.

Image analysis

Analysis of all magnetic resonance images was performed on a PACS workstation monitor by an experienced radiologist with more than ten years of experience in the interpretation of abdominal MRI. The observer was blinded to pathological results and the clinical history of the patients. Images were reviewed for the general characteristics of the lesions on T1-weighted, T2-weighted and diffusion-weighted images, and enhancement patterns on post-contrast T1-weighted images. The quantitative analysis of diffusion (i.e., ADC) was calculated on a PACS workstation by applying ROI on the image. In the case of tumors with necrotic/cystic areas, the ROI was applied to the tumor's non-necrotic portion. T2-weighted and diffusion-weighted images were reviewed to determine any difference in lesion characterization. In order to reduce recall bias, T2-weighted and diffusion-weighted images were randomly analyzed in two different sessions separated by at least two weeks. As seen on T2-weighted images, if the lesion had a sharp margin and a round or oval shape and was homogenously hyperintense, it was considered benign. On the other hand, if the lesion had an indistinct margin and an irregular shape and was only slightly hyper-intense or iso-intense as seen on T2-weighted images, it was considered malignant. On diffusion-weighted images, if the lesion was hyper-intense on b=50 s/mm^2 image and showed decreased signal intensity or a decreased size of the lesion on b=800s/mm^2 image, it was considered as benign. On the other hand, if the lesion had the same or increased signal intensity or an increased size on b=800 s/mm^2 image rather than on b=50 s/mm^2 image, it was considered malignant. Sensitivity, specificity, and accuracy for T2-weighted and DWI were calculated. The sensitivity, specificity, and accuracy of T2-weighted images were compared with those of diffusion-weighted images.

The final diagnosis was confirmed by histopathology/cytology (n=107). In cases where histopathology/cytology was not available, the diagnosis was confirmed by characteristic imaging findings along with ultrasonographic follow-up at six months for any increase in lesion size (n=37) or any other relevant investigation (e.g., tumor markers, RBC Scan) (n=15).

Statistical analysis was performed using SPSS software

(version 20.0). A *P* value was considered significant at <0.05. Kappa analysis was utilized to determine the agreement between T2-weighted images, diffusion-weighted images, and final diagnosis (standard of reference). ROC analysis was used to determine the optimal ADC and T2 relaxation threshold values for lesion discrimination, and corresponding sensitivities, specificities, and accuracy were calculated.

Results

Our study was prospective with a duration of over one year (2019-2020). The study included 159 patients with USG documented focal liver lesions. After proper clinical evaluation and work-up as per set Performa, all patients underwent MRI.

The final diagnosis was confirmed by histopathology/cytology (n=107). In cases where histopathology/cytology was not available, the diagnosis was confirmed by characteristic imaging findings along with ultrasonographic follow-up at six months for any increase in lesion size (n=37) or any other relevant investigation (e.g., tumor markers, RBC Scan) (n=15). In 37 patients whom the final diagnosis was reached upon by characteristic imaging findings and ultrasonographic follow-up, the mean duration of follow-up was 12.9 months (range of 6-17 months).

Distribution of benign and malignant lesions as per final diagnosis:

Out of the 159 cases in our study, 92 (57.8%) had benign lesions whereas 67 (42.2%) turned out to be malignant. The benign lesions included hemangioma [63 (68.4%)], FNH [7 (7.6%)], hepatic adenoma [8 (8.6%)], hydatid cyst [12 (13.0%)], simple cyst [1 (1.0%)] and angiomyolipoma [1 (1.0%)]. The malignant lesions included metastasis [38 (56.7%)], hepatocellular carcinoma [18 (26.8%)], cholangiocarcinoma [9 (13.4%)] and hepatoblastoma [2 (2.9%)].

Age

The mean age of patients was 43.4 ± 16.5 years. The mean age of patients with benign lesions was 39 ± 12.9 years, compared to 51 ± 19.3 years for patients with malignant lesions.

Gender

In our study, 71 patients (44.7%) were males, and 88 patients (55.3%) were females. Among the patients with benign lesions, 36 patients (39.1%) were males, whereas 56 patients (60.9%) were females. Among the patients with malignant lesions, 35 patients (52.2%) were males, whereas 32 patients (47.8%) were females.

Size of the lesions

The mean size of benign lesions was 5.9 cm as compared to 6.6 cm for malignant lesions. On statistical analysis, no significant difference was seen between benign and malignant lesions regarding the lesion size ($P = 0.493$).

MRI characteristics

T1-weighted imaging characteristics

The T1 characteristics of benign lesions included low signal in 64, intermediate in 9 and high signal in 10 patients. Nine benign lesions also showed a high signal that showed a decrease in out-of-phase images suggestive of fat. The malignant lesions, on the other hand, were low signal (51), intermediate (13), and high signal in 3 patients.

T2-weighted imaging characteristics

The T2 characteristics of benign lesions included low signal in 4, intermediate in 9, and high signal in 72 patients. Seven benign lesions showed a heterogeneous signal. On the other hand, the malignant lesions had low signal (0), intermediate (53), and high signal in 8 patients. Six malignant lesions showed heterogeneous signal intensity.

Additional features on T2 weighted imaging

Additional T2 weighted imaging features which helped in specific diagnosis were sought, and we found hyper-intense central scar in 5 patients with benign FNH, hypo-intense central scar in 4 patients with Fibrolamellar HCC, and hypo-intense rim on T2W imaging in 3 patients with hydatid cyst, and one patient with HCC.

Long-TE T2-weighted images

The character of each lesion on increasing TE images was recorded both qualitatively and quantitatively (Table 1).

Diffusion weighted imaging

Mean ADC values of benign and malignant lesions are available in Table 2.

On statistical evaluation, there was a highly significant difference between the ADC values of benign and those of malignant lesions ($P < 0.001$).

The ADC value for each type of lesion was also calculated and is given in Table 3.

ROC curve analysis for lesion characterization

ROC curve analysis was done to obtain a threshold for differentiating benign from malignant and also various lesions among themselves (Figure 1).

Accuracy of T2 weighted imaging

We found that T2 weighted imaging was able to correctly classify 82.0% (i.e., 55 out of 67) of the lesions as malignant and 83.7% (i.e., 77 out of 92) of the lesions as benign.

Accuracy of DWI

On diffusion-weighted imaging, 89.5% (i.e., 60 out of 67) of the lesions were correctly classified as malignant, and 88.0% (i.e., 81 out of 92) of the lesions were correctly

Table 1. Showing the change in the signal of the lesions with increasing TE on T2 weighted imaging

Lesion Type	High signal	Low/intermediate signal
Haemangioma	58	5
FNH	1	6
Hepatic adenoma	0	8
Angiomyolipoma	0	1
Hydatid cyst	2	10
Simple cyst	1	0
Metastasis	2	36
HCC	0	18
Cholangiocarcinoma	0	9
Hepatoblastoma	0	2
Total	**63**	**104**

FNH, fibronodular hyperplasia; HCC, hepatocellular carcinoma.

classified as benign.

Comparison of T2-weighted and diffusion-weighted imaging in lesion characterization

On comparing T2-weighted and DWI for lesion characterization, there was no statistically significant difference in the sensitivity, specificity, and accuracy between the results obtained using T2-weighted and DWI (p = 0.546) (Table 4).

Discussion

In the current study, 159 patients with focal liver lesions detected on USG were evaluated using MRI with the aim of lesion characterization and differentiating benign from malignant lesions. The final diagnosis was confirmed by histopathology/cytology (n=107). In cases where histopathology/cytology was not available, the diagnosis was confirmed by characteristic imaging findings along with ultrasonographic follow up at six months for any increase in lesion size (n=37) or any other relevant investigation (e.g., tumor markers, RBC Scan) (n=15) as was done in previous studies.[16-19] The mean duration of follow-up in our study was 12.9 months (range of 6 to 17 months).

Out of the 159 cases in our study, 92 (57.8%) had benign lesions, whereas 67 (42.2%) turned out to be malignant. Our study is one of the largest studies on liver lesions in our region.

Patients in our study had a mean age of 43.4 years. Patients with benign liver lesions had a mean age of 39 ± 12.9 years, while those with malignant lesions had a mean age of 51 ± 19.3 years. There was a statistically significant

Table 2. Showing the mean ADC value of each type of lesion with values higher in benign lesions while lower values are seen in malignant lesions

Lesion Type	N	Range of ADC values ($\times 10^{-3}$ mm²/s)	Mean ADC value ($\times 10^{-3}$ mm²/s)	Standard deviation	Standard error of mean
Benign	92	1.20 - 2.65	1.68	0.33	0.06
Malignant	67	0.64 - 1.32	1.05	0.21	0.05

ADC: Apparent Diffusion Coefficient. Independent t-test ($p < 0.001$); highly significant

Table 3. Showing the mean ADC of each type of lesion in the study

Lesion Type	N	Range of ADC values ($\times 10^{-3}$ mm²/s)	Mean ADC value ($\times 10^{-3}$ mm²/s)	SD
Haemangioma	63	1.40 - 2.40	1.71	0.26
FNH	7	1.40 - 1.56	1.47	0.82
Hepatic adenoma	8	1.28 - 1.35	1.31	0.49
Angiomyolipoma	1	1.45	1.45	-
Hydatid cyst	12	1.20 - 2.10	1.65	0.64
Simple cyst	1	2.65	2.65	-
Metastasis	38	0.64 - 1.20	0.92	0.18
HCC	18	0.80 - 1.32	1.07	0.23
Cholangiocarcinoma	9	1.15 – 1.25	1.21	0.45
Hepatoblastoma	2	1.28	1.28	-

ADC: Apparent Diffusion Coefficient. SD: Standard Deviation.

Table 4. Showing a comparison of the accuracy of T2WI and DWI in differentiating benign and malignant focal liver lesions

MR Imaging	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)
T2-weighted imaging	82.0	83.7	82.9	75	89.6
Diffusion-weighted imaging	89.5	88.0	88.7	80	93.1

PPV, positive predictive value; NPV, negative predictive value.
Z-test (test of proportions): Z = -0.60, *P* = 0.546 (not significant).

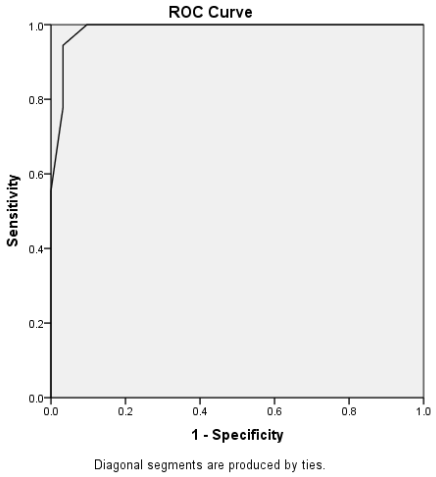

Figure 1. ROC curve for calculation of ADC threshold to differentiate benign from malignant liver lesions.

difference between the age of presentation of benign and malignant lesions ($P < 0.05$), indicating that patients with advanced age have a greater malignancy chance. Regarding the sex of the study group, 71 (44.6%) patients were males, and 88 (55.4%) were females.

The mean size of the liver lesions in our study was 6.2 ± 2.9 cm (range of 0.9 to 12.6 cm). Benign lesions had a mean size of 5.9 ± 3.1 cm (range of 0.9 to 12.6 cm), whereas malignant lesions had a mean size of 6.6 ± 2.8 cm (range of 1.6 to 12 cm). There was no significant difference between the size of benign and malignant lesions ($P < 0.05$) on statistical analysis.

MRI characteristics

T1 weighted imaging

Among the benign lesions, 64 lesions appeared uniformly hypo-intense, 9 showed intermediate signal, and 10 showed high signal foci. Among these 10 lesions, 9 (8 adenomas and one angiomyolipoma) showed a signal loss on out of phase T1-weighted images suggesting the presence of fat. In contrast, one lesion (adenoma) showed persistent high signal even on out of phase T1-weighted images suggesting intra-lesional hemorrhage. Among the malignant lesions, 51 showed uniform low signal, 13 had intermediate signal, and three lesions had high signal on T1-weighted images (which turned out to be hemorrhagic metastasis). The difference in T1 signal between benign and malignant lesions was not statistically significant ($P > 0.5$). T1 images, however, can be helpful in some instances, like detecting fat, hemorrhage, or iron deposition. A T1 hyperintense lesion must be subjected to T1-weighted in and out of phase imaging. Three possibilities can arise, giving us a sense of lesion's nature: no change in signal between 2 phases suggesting hemorrhage within the lesion, loss of signal on out of phase imaging suggesting fat within the lesion, and loss of signal on in-phase images suggesting iron deposition. These features may aid in diagnosis but cannot differentiate benign from malignant lesions as they can occur in either of these lesions. These findings have been corroborated in many previous studies,

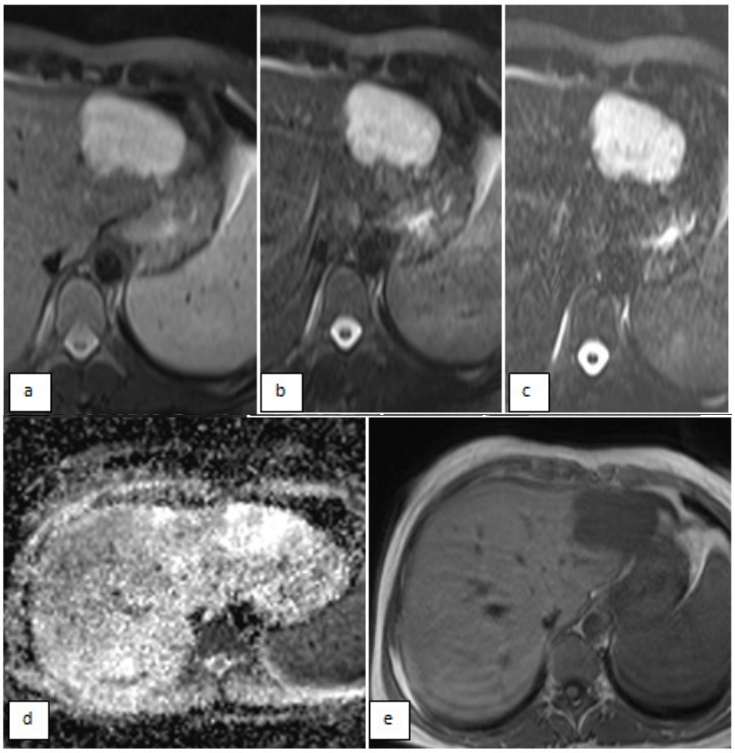

Figure 2. T2 weighted images with increasing TE (a, b, c) showing increasing signal intensity of left lobe haemangiomas owing to its high fluid content. ADC map (d) showing free diffusion in the lesion pointing to its benignity [ADC = 1.89×10^{-3} mm²/s]. T1 weighted image (e) showing a well-defined hypointense lesion in the left lobe.

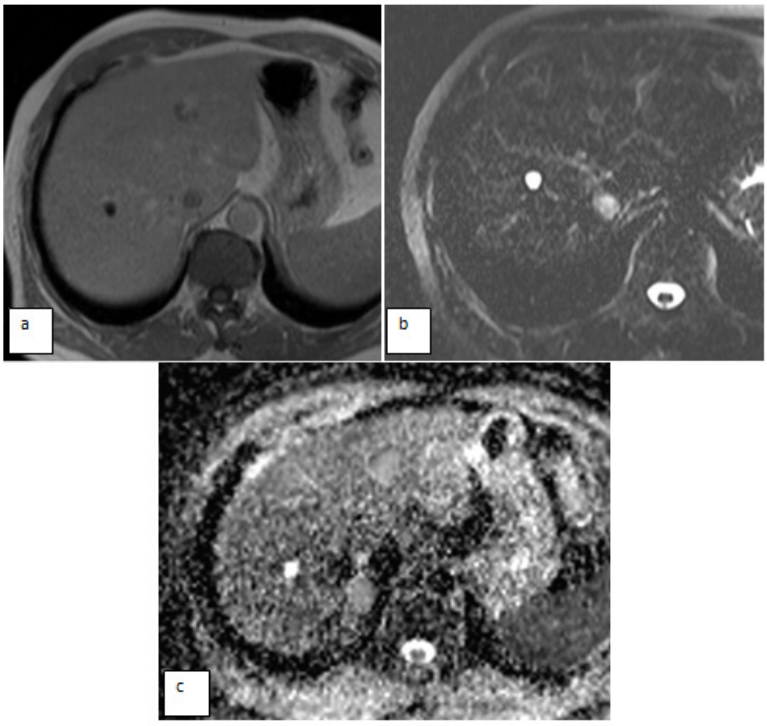

Figure 3. T1 weighted image (a) showing a well-defined uniformly hypointense lesion in the right lobe. Long TE (279 msec) T2 weighted image (b) showing a bright hyperintense lesion suggestive of a high fluid content cyst. ADC map showing free diffusion in the lesion with an ADC value of 2.65×10^{-3} mm^2/s.

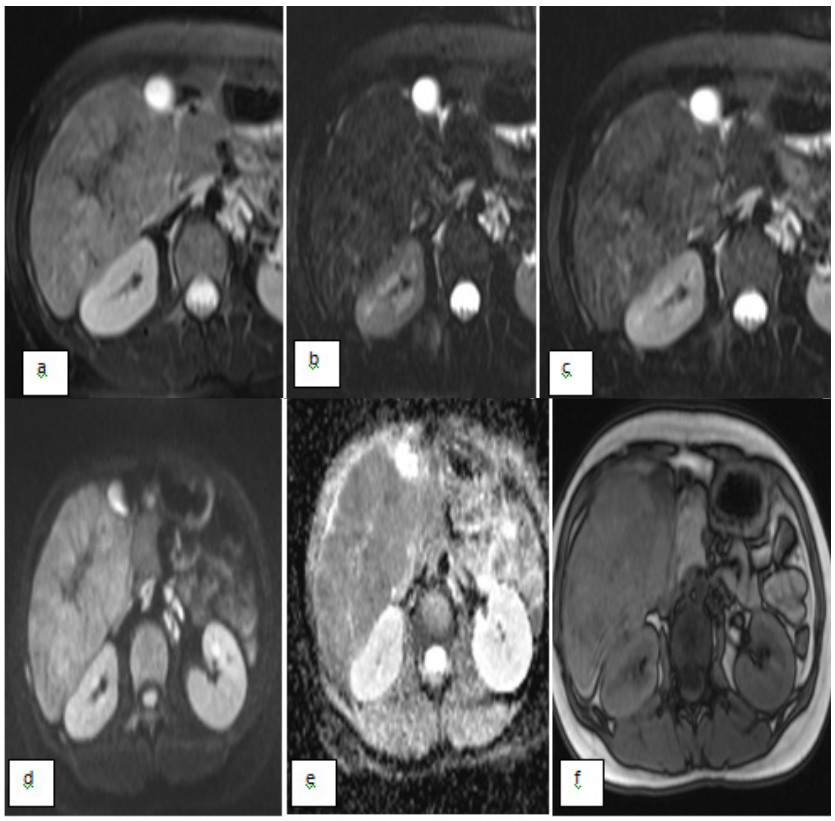

Figure 4. Increasing TE T2 weighted images (a, b, c) showing a decrease in signal intensity of a large right lobe lesion in comparison to GB, which increases in signal intensity, indicating a solid lesion. A central T2 hypointense scar can also be noted (a). DWI (d) and ADC map (e) showing that the lesion shows strong diffusion restriction (ADC=0.95×10^{-3} mm^2/s), indicating a malignant lesion. T1 weighted image (f) showing a large heterogenous iso-hypo intense mass lesion in the right lobe of the liver. On histopathology, this lesion was found to be a fibrolamellar variant of HCC.

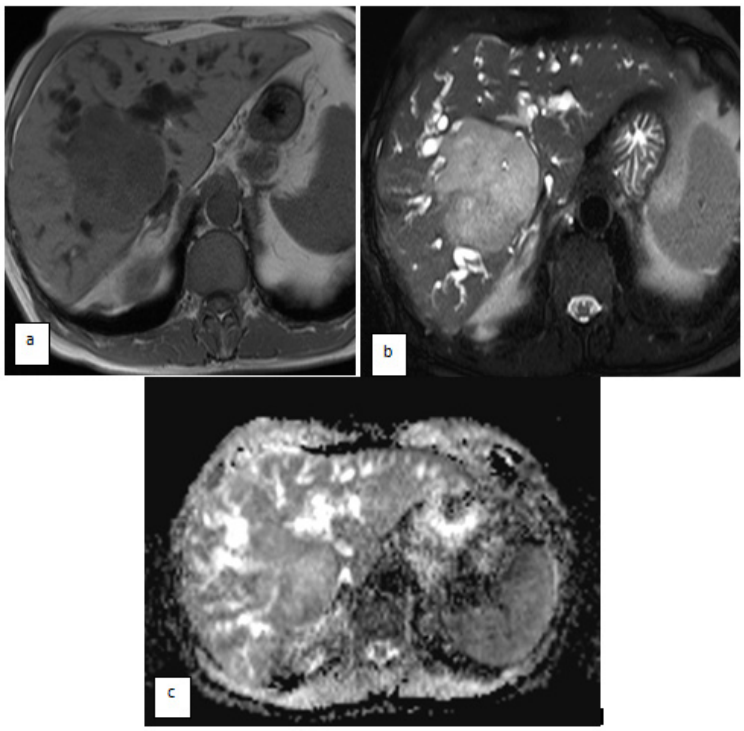

Figure 5. T1 weighted image (a) showing a large central hypointense lesion which is hyperintense on T2 weighted image (b) and is causing marked dilatation of intrahepatic biliary radicles. ADC map(c) showing diffusion restriction within the lesion with ADC value of 1.17×10^{-3} mm^2/s. On histopathology, this was found to be a mass-forming cholangiocarcinoma.

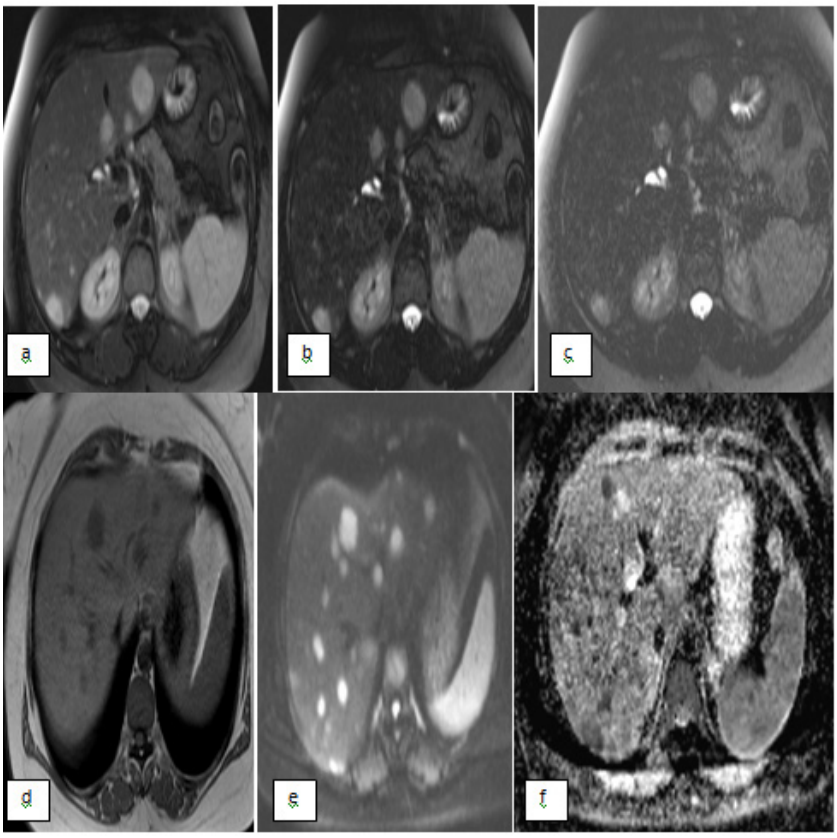

Figure 6. Increasing TE T2 weighted images (a, b, c) in a patient with known carcinoma colon and a solitary lesion on USG. With increasing TE, the signal intensity of the lesions does not increase, indicating a solid lesion. T1 weighted image showing the lesions as hypointense in relation to liver parenchyma. DWI and ADC map showing additional lesions as well as strong diffusion restriction indicating metastatic nature of the lesions. The ADC value calculated in one of the lesion was 0.72×10^{-3} mm^2/s

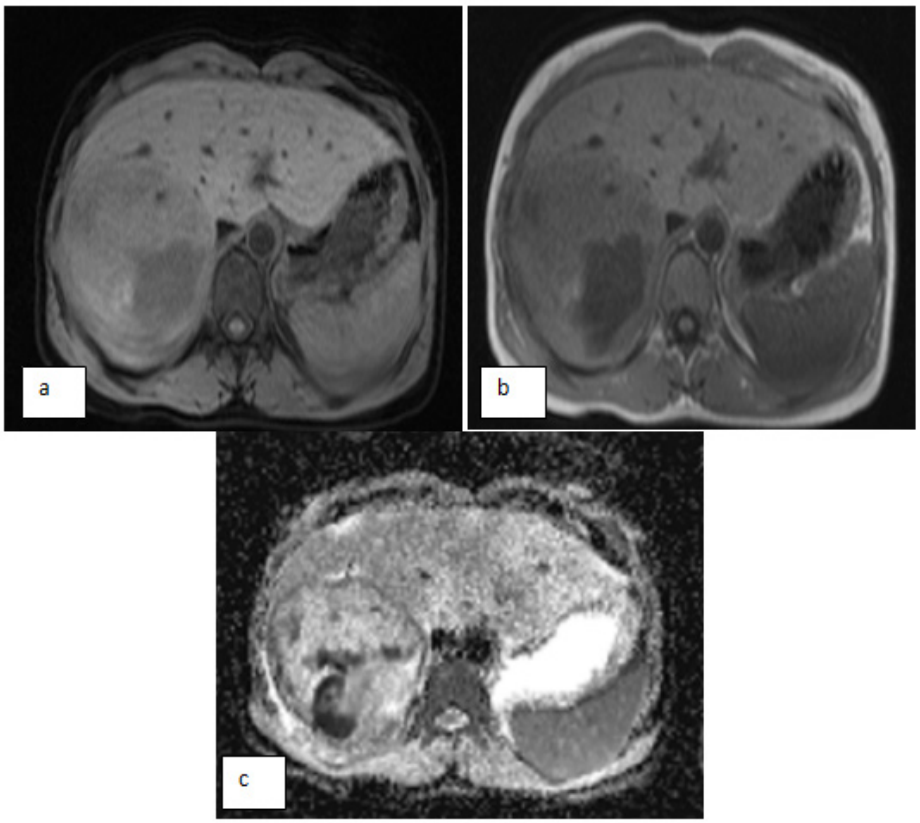

Figure 7. T1 weighted in phase and out of phase images (a,b) showing a large right lobe lesion which is heterogeneous with areas of T1 hyperintensity, which shows a drop in signal on out of phase image (b) suggesting intralesional fat. ADC map (c) showing the heterogenous nature of the lesion with few areas of diffusion restriction. The ADC value of the restricting area was 1.29×10^{-3} mm^2/s. This turned out to be hepatic adenoma on histopathology.

including those by Matsui et al[20] and Merkle et al.[21]

T2 weighted imaging

Most benign lesions (72) were uniformly hyperintense on T2-weighted imaging, 9 had intermediate signal (4 haemangiomas and 5 FNH), 7 had heterogeneous signal (2 FNH and 5 adenomas), and 4 benign lesions had low signal (hydatid cysts). Only 8 had uniformly high signal among the malignant lesions, 53 had intermediate signal, and 6 had heterogeneous signal. The difference in T2 signal characteristics was statistically significant ($P<0.05$). This shows that T2 signal of the lesion can indicate its benign or malignant nature, however with some exceptions as indicated. We found that T2 weighted imaging correctly classified 82.0% (i.e., 55 out of 67) of the lesions as malignant and 83.7% (i.e., 77 out of 92) of the lesions as benign. Those misclassified as benign included 10 cases of metastases and 2 cases of hepatocellular carcinoma, whereas 6 cases of hemangiomas and 3 cases each of hydatid cyst, hepatic adenoma, and FNH were misclassified as malignant on T2-weighted imaging. Our findings are in accordance with the findings of Parikh et al [12] and Yang et al.[18] Thus, T2 weighted imaging provides an initial road map to classify a lesion as benign or malignant.

We also looked for some additional characteristic imaging features on T2 weighted imaging, which helped us reach a definitive diagnosis. We found a hyper-intense central scar in 5 cases (which turned out to be FNH on histopathology). Hypointense central scar was seen in 4 cases of hepatocellular carcinoma (fibrolamellar variant). Peripheral hypo-intense capsule on T2-weighted images was seen in 3 cases of hydatid cyst and one case of hepatocellular carcinoma. Thus, the central scars' character, although not absolute but helps in a great way to reach the diagnosis of FNH or fibrolamellar variant of HCC.

Role of long TE T2-weighted imaging in lesion characterization

In our study, most of the hemangiomas (92.0%) showed a high signal with increasing TE values on T2-weighted images compared to metastases in which only 2 cases (5.2%) showed high signal with increasing TE values. None of the cholangiocarcinoma and hepatocellular carcinoma cases showed increased signal with increasing TE values on T2-weighted images (Table 1). There was a highly significant difference between imaging characteristics of hemangiomas and metastases on long-TE T2-weighted imaging ($P<0.001$) on statistical analysis. Also, there was a significant difference between hemangiomas and

hepatocellular carcinomas ($P < 0.001$). Our findings are in concordance with previous studies by Caseiro-Alves et al,[22] Vilgrain et al,[23] McFarland et al,[15] and Kim et al.[24] This indicates a significant role of long TE T2 weighted images in differentiating benign lesions (haemangioma and cysts) from metastatic lesions, especially in patients with a known primary where exclusion of metastasis can greatly alter the management. However, a few exceptions should be kept in mind, including the metastasis from carcinoid, renal cell carcinoma, and melanoma, which can sometimes show high signal as was seen in 2 of our cases (both metastasis from renal cell carcinoma) owing to their high fluid content.

Diffusion-weighted imaging

In our study, the mean ADC value of benign lesions was $1.68 \pm 0.33\times10^{-3}$ mm²/s as compared to malignant lesions, which had a mean ADC value of $1.05 \pm 0.21\times10^{-3}$ mm²/s (Table 2). On statistical evaluation, we found a highly significant difference between the ADC values of benign and those of malignant lesions ($P < 0.001$). Our findings are in line with those of Gourtsoyianni et al[25] [benign lesions (2.55×10^{-3} mm²/s) and malignant lesions (1.04×10^{-3} mm²/s)], Demir et al[26] [benign lesions ($2.57 \pm 0.26 \times 10^{-3}$ mm²/s) and malignant lesions ($0.86 \pm 0.11\times10^{-3}$ mm²/s)] and Namimoto et al[27] [malignant masses (1.04×10^{-3} mm²/s) and benign masses (hemangiomas [1.95×10^{-3} mm²/s] and cysts [3.05×10^{-3} mm²/s]). Similar findings were also observed by Bruegel et al,[10] Taouli et al,[11] and Holzapfel et al[28] in their studies. Thus DWI with ADC values can discriminate benign from malignant lesions comprehensively. Also, we found that in patients with single metastasis on USG or CT, many additional lesions were found on DWI, thereby changing the management of the patient significantly. Thus DWI is a sine qua non as far as liver lesion assessment is concerned.

By plotting the ROC curve, we obtained a threshold ADC value that gave the most accurate result as far as differentiating benign from malignant lesions. Using a threshold ADC value of 1.37×10^{-3} mm²/s, 89.5% (i.e., 60 out of 67) lesions were correctly classified as malignant, and 88.0% (i.e., 81 out of 92) lesions were correctly classified as benign. Those misclassified as benign included 3 cases of hepatocellular carcinomas and 4 cases metastasis, whereas 5 cases of hemangiomas, 2 cases of hydatid cyst, and four hepatic adenomas were misclassified as malignant on DWI. We, therefore, put forth an ADC value based on our large study population that can help differentiate benign from malignant liver lesions with sufficient accuracy. Our findings closely match those of Taouli et al[11] – 1.5×10^{-3} mm²/s, Bruegel et al[10] – 1.63×10^{-3} mm²/s, Holzapfel et al[28], Battal et al[29] –1.21×10^{-3} mm²/s,– 1.41×10^{-3} mm²/s and Kim et al[16] – 1.6×10^{-3} mm²/s.

In addition to differentiating benign from malignant lesions, we also sought ADC threshold values for discriminating certain individual lesions (Table 3). In differentiating hemangiomas and metastases, a threshold value of 1.40×10^{-3} mm²/s gave a maximum sensitivity, specificity, and accuracy of 93%, 89%, and 88%, respectively. This, when combined with a long TE image, gave an accuracy of 100%. In his study, Bruegel et al[10] found a maximum sensitivity, specificity, and accuracy of 84%, 82%, and 83%, respectively, for differentiating hemangiomas from metastases at a threshold ADC value of 1.57×10^{-3} mm²/s. The lower threshold value in our study is likely a result of the lack of cystic metastatic lesions in our study, which tend to have higher ADC values. Also, there was no overlap between the ADC values of hemangiomas and simple cyst, giving a 100% sensitivity, specificity, and accuracy for differentiating the two at a threshold value of 2.4×10^{-3} mm²/s. The higher ADC value of cysts has been documented in previous studies.[26,30] No previous attempt to obtain a threshold ADC for differentiating haemangiomas from cysts has been made to our knowledge. This can help solve the dilemma of T2 hyperintense lesions by providing a quantitative assessment of these lesions (Table 5).

Although metastases showed a slightly lower mean ADC (0.92×10^{-3} mm²/s) as compared to HCC's (1.07×10^{-3} mm²/s), a statistically significant difference was not observed ($P = 0.24$). These results are consistent with previous studies.[10,31] In our study, although solid benign liver lesions (FNH and adenoma) had lower ADC values as compared with other benign lesions (hemangiomas and cysts), the results did not reach statistical significance ($P = 0.135$). These results are also consistent with Bruegel and colleagues' study.[10]

Comparison between DW imaging and T2-weighted imaging for lesion characterization

In our study, T2-weighted imaging had a sensitivity, specificity, and accuracy of 82.0%, 83.7%, and 82.9% for lesion characterization with a positive predictive value for malignancy of 75% and a negative predictive value of 89.6%. The agreement of final diagnosis (standard of reference) with T2-weighted images was statistically significant ($P < 0.001$). DWI had a sensitivity, specificity, and accuracy of 88.9%, 87.1%, and 87.7% for lesion characterization with a positive predictive value for malignancy of 80% and a negative predictive value of 93.1%. On comparing the diagnosis on DWI with the final diagnosis (standard of reference), there was a significant agreement between the two ($P < 0.001$). These findings are concordant with those of Parikh et al[12] and Yang et al.[18] Also, in our study, although the accuracy of DWI was numerically higher than that of T2-weighted images, there was no statistically significant difference (Table 6) between the results obtained with the use of T2-weighted and DWI ($P > 0.05$), which is also consistent with previous studies.[12,18] However, the superior lesion detection capabilities of DWI, including the ability to detect lesions not seen on any other imaging, especially in metastasis, making it a superior and essential MRI sequence in

Table 5. Showing the general characteristics and mean ADC values among the benign and malignant group of patients

Characteristic	Benign	Malignant
Mean age (y)	39 ± 12.9	51 ± 19.3
Gender(male/female ratio)	39.1%/60.9%	52.2%/47.8%
Mean lesion size (cm)	5.9 cm	6.6 cm
Mean ADC value ($\times 10^{-3}$ mm^2/s)	1.68	1.05

Table 6. Showing the ADC thresholds for differentiating malignant from benign as well as haemangiomas for cysts based on ROC curve analysis.

	Threshold ADC ($\times 10^{-3}$ mm^2/s)	Sensitivity (%)	Specificity (%)	Accuracy (%)
Malignant vs benign lesions	1.37	100%	90.3%	93.8%
Haemangioma vs metastasis	1.4	100%	100%	100%
Metastasis vs cyst	1.2	100%	100%	100%

evaluating focal liver lesions.

Conclusion

- MRI is an excellent modality for depicting the characteristic imaging features of focal liver lesions, which aids correct diagnosis.
- Heavily T2-weighted imaging (with long TE values) was able to accurately differentiate between hemangiomas and metastases ($P < 0.05$) without the need for contrast administration.
- DWI is a sine qua non for focal liver lesion assessment and helps discriminate benign and malignant hepatic lesions and pick up additional lesions.
- Quantitative ADC measurement is highly sensitive, specific, and accurate for differentiating malignant from benign lesions at a threshold ADC value of 1.37×10^{-3} mm^2/s.

Conflict of Interest

Authors declare no conflict of interest in this study.

Ethical Approval

The study was approved by the Ethical Committee SKIMS, Soura, J&K, INDIA.

Study Highlights

What is current knowledge?

- MRI has long been used for characterization of the liver lesions, however the assessment is subjective and may sometimes be difficult.

What is new here?

- Our study provides objective numbers in the form of threshold ADC values for differentiating not only benign and malignant lesions but also individual lesions. ADC value ranges of most of the liver lesions have also been assesed.

Authors' Contribution

OA: Design, compilation, patient image acquisition, and assessment. NC: Design, data collection. OS: Data collection, analysis, writing of paper.

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