Assessment of LI-RADS Efficacy in the Classification of Hepatocellular Carcinoma and Benign Liver Nodules Using DCE-MRI Features and ADC MRI

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Abstract- The Liver Imaging Reporting and Data System (LI-RADS) is a widely utilized tool for classifying liver lesions, particularly in patients at risk for hepatocellular carcinoma (HCC). This study aims to assess the efficacy of LI-RADS in distinguishing between HCC and benign liver nodules by leveraging dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) features and apparent diffusion coefficient (ADC) values derived from MRI. Between October 2023 and March 2024, 43 patients with suspected HCC underwent MRI evaluation, including DCE-MRI and DWI sequences. The diagnostic performance of various MRI sequences was analyzed, focusing on their ability to differentiate HCC from benign lesions. The diagnostic efficacy of DCE-MRI and ADC in differentiation was evaluated using statistical analyses, such as t-tests and receiver operating characteristic (ROC) curve analysis. SPSS VER 16 was used to analyze the collected data. The study findings reveal that the DCE-MRI arterial phase demonstrated perfect diagnostic accuracy with an area under the curve (AUC) of 1.00, achieving 100% sensitivity and specificity. T2-weighted imaging also exhibited diagnostic solid performance, with an AUC of 0.801, while ADC values from DWI sequences showed limited efficacy in differentiating HCC from benign lesions (AUC=0.512). These findings indicate that DCE-MRI significantly enhances the accuracy of LI-RADS in classifying HCC versus benign liver nodules. This study highlights the importance of incorporating advanced imaging features into LI-RADS to improve the diagnostic precision of liver lesion evaluation in clinical practice.

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Introduction

Hepatocellular carcinoma (HCC) is the most common type of liver cancer, accounting for nearly 90% of all cases (1). HCC is becoming increasingly common worldwide, with over 700,000 new patients diagnosed yearly. A serious health problem can lead to significant morbidity and mortality (2). HCC is a complex, disorderly state involving multiple events and etiologies, typically viral hepatitis and metabolic syndrome. Intriguingly, the incidence of HCC in men is four times that in women (3). The occurrence of HCC is often associated with multiple risk factors, such as persistent infection with the hepatitis virus, chronic alcohol consumption, and aflatoxin B1 exposure (4). Additionally, metabolic disorders such as diabetes and obesity are also considered risk factors for liver cancer. Regardless of etiology, the neoplastic lesion usually originates on a bed of chronic necroinflammation that sequentially progresses from fibrosis to cirrhosis and culminates in HCC (5).

Iraq has one of the highest incidence rates of HCC among Middle Eastern countries, with varying rates between regions. Based on the Global Cancer Observatory in IRAQ 2020, Iraq's age-standardized incidence rate (ASR) HCC was estimated to be 3.3 per 100,000 in 2020. According to the GLOBOCAN 2021 data, there were 713 new cases of liver cancer reported in Iraq, of which 361 were male and 352 were female. The mortality rate of HCC in Iraq is also high, with an ASR

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of 3.2 per 100,000 in 2020 (6).

The Liver Imaging Reporting and Data System (LI-RADS) has emerged as a standardized tool for the diagnosis and classification of HCC and other liver lesions, primarily using imaging modalities such as dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) (7). LI-RADS aims to improve diagnostic accuracy by categorizing liver nodules based on specific imaging features, facilitating consistent communication among radiologists, hepatologists, and oncologists (8). A crucial aspect of this system's efficacy is its ability to distinguish between malignant and benign liver lesions, which has significant implications for patient management and treatment outcomes (9,10).

This study focuses on assessing the efficacy of LI-RADS in differentiating HCC from benign liver nodules, utilizing both DCE-MRI features and apparent diffusion coefficient (ADC) values from MRI. DCE-MRI provides detailed information on the vascular characteristics of liver lesions, which are vital for identifying HCC, while ADC values offer additional insights into the tissue cellularity and integrity of the lesions. By evaluating the performance of LI-RADS in the context of these advanced imaging techniques, this study aims to determine the accuracy and reliability of the system in clinical practice, potentially guiding improvements in liver cancer diagnosis and treatment strategies.

Materials and Methods

Patient

This prospective single-center study obtained approval from Alayen Iraqi University AUIQ (Ethical Code: AUIQ-A25001). Written consent from patients was obtained. All the patients with liver nodules without prior treatment, including surgery or chemotherapy, were included in the study. A radiologist assessed MRI image quality with 12 years of experience in diagnostic imaging, and a score of 43 cirrhotic masses was classified with LI-RADS scoring from 2-5. To classify lesions into benign and HCC, we used pathology results for LI-4 & LI-5 lesions and 12-month imaging follow-up for LI- 2 & LI-3 lesions.

The inclusion criteria for the study encompassed patients with risk factors for HCC and hepatic cirrhosis who underwent diagnostic MRI using an extracellular contrast agent and ADC analysis. Patients were required to have a pathological diagnosis obtained through surgical resection, liver biopsy, or liver transplantation. Lesions classified as benign were confirmed by follow-up imaging performed at least one year after the initial examination used for the LI-RADS assessment, demonstrating stable or reduced lesion size. Preoperative treatments were noted, including percutaneous ethanol injection, radiofrequency ablation, chemoembolization, or combinations thereof. Exclusion criteria included the absence of complete pathological results, poor image quality due to motion artifacts or metal interference, and prior LI-RADS assessments before the initiation of treatment for the liver lesion

MR examinations

MRI was conducted using a 3T MRI scanner (GE Medical Systems, Discovery 750w 3T) at a single imaging center. The imaging protocols included the following sequences:

Diffusion-weighted imaging (DWI) was performed with three orthogonal directions using respiratory-triggered 2D echo planar imaging (EPI) with three b-values (0, 200, 800 s/mm^2) before the administration of the contrast agent. The ADC for the region of interest (ROI) was calculated on a dedicated workstation.

DCE-MRI was conducted using a liver acquisition with volume acceleration (LAVA) sequence, a 3D spoiled gradient-recalled echo (SPGR) sequence with uniform fat suppression. This sequence was performed in the axial plane with a breath-hold 2D gradient echo T1-weighted sequence. Data acquisition commenced 10 seconds before the contrast agent injection to capture baseline signal intensity. Dynamic contrast-enhanced images were obtained with a temporal resolution of 4 seconds per image across six acquisition phases during normal breathing. T2-weighted imaging used a single-shot fast spin echo (SSFSE) sequence. Detailed information regarding the imaging protocol can be found in Table 1.

Patient and method

A prospective computerized search was conducted to identify all subjects who underwent liver MRI between October 2023 and March 2024. This search yielded 43 patients (27 men and 16 women, aged 43-70 years) referred to our institution for an initial evaluation via liver MRI. Notably, none of these patients had received prior medical or interventional treatments. The Ethics Committee of Alayen Iraqi University (AUIQ) approved the study.

Data collection

Following ethical approval from Alayen Iraqi University (AUIQ), we identified 43 patients (27 men and 16 women, aged 43-70 years) referred to our institution

between October 2023 and March 2024. Initially assessed using ultrasound and liver CT scans, these patients underwent unenhanced liver MRI for further evaluation. The MRI findings were compared with histopathological results or follow-up imaging, which served as the reference standard. Data were entered and analyzed using SPSS version 26.

During the five-month study period, we collected data from 43 patients referred to our institution from various medical and surgical departments, including the oncology unit. Each patient underwent a thorough clinical history review, general liver examination, laboratory tests, and liver MRI.

Image analysis

All measurements were conducted on a Picture Archiving and Communication System (PACS) workstation. A radiologist assessed MRI image quality with 12 years of experience in diagnostic imaging which classified 43 cirrhotic masses using the LI-RADS scoring system, ranging from categories 2 to 5, to distinguish between benign lesions and HCC. Image interpretation was performed by a radiologic technologist, Hayder Suhail Najm, with 13 years of experience in hepatobiliary imaging and 8 years of experience in interpreting DCE-MRI and ADC features, as well as a radiology technology student with two years of training, including expertise in interpreting DWI images and ADC maps. The investigators were blinded to the patient's clinical and pathological information.

ADC maps were generated from the DWI sequence. ADC values for each lesion were obtained using region of interest (ROI) analysis. Continuous sections were thoroughly inspected, including the enhancing tumor and peritumoral region. For ROI analysis, a minimum of five sections were selected. Within the intratumoral region, 5–8 ROIs were placed in the solid portions of the tumor, carefully avoiding hemorrhagic, cystic, and necrotic areas. The ROI diameters ranged from 10 to 120 mm², depending on the tumor's size and morphology. The ROI with the lowest ADC value was identified as the minimum ADC (ADCmin), while the mean ADC (ADCmean) was calculated from multiple ROIs.

The peritumoral region was defined as the area adjacent to the solid part of the lesion. At least 2-3 ROIs (100 mm² each) were positioned as close to the tumor margin as possible, using T1-weighted post-contrast images as references. The ROI with the lowest ADC value in this region was selected as the minimum ADC for edema (ADCedema). In discrepancies between investigators, consensus was reached to determine an average ADC value (Figure 1).

Statistical analysis

We used SPSS, t, and chi-square methods to analyze statistical data. A $P<0.05$ was considered a significant level in all results. Diagnostic indices of MR imaging methods were calculated based on sensitivity, specificity, positive and negative predictive values, and positive and negative likelihood ratios.

Diagnostic indices calculation

Sensitivity: Defined as the proportion of true positive cases (correctly identified HCC) among all patients. It is calculated using the formula:

$$\text{Sensitivity} = \frac{\text{True Positives}}{\textit{True Positives} + \textit{False Negatives}} \times 100\%$$

Specificity: Indicates the proportion of true negative cases (correctly identified benign liver nodules) among all individuals. It is calculated as follows:

$$\text{Specificity} = \frac{\text{True Negatives}}{\textit{True Negatives} + \textit{False Positives}} \times 100\%$$

Predictive Value (PPV): Represents the probability that a patient with a positive test result truly has HCC.

Negative Predictive Value (NPV): Indicates the probability that a patient with a negative test result truly does not have HCC.

Table 1. MR protocols

Sequence	TR (ms)	TE (ms)	FA (°)	Section thickness (mm)	Matrix	FOV (mm2)
T1-weighted 3D GRE NAV	100	4.2	24°	2	280 × 400	280 × 380
T2-weighted FSE	538	110	90°	5	320 × 320	380 × 380
T1-weighted dual-echo 3D GRE	4.1	1.3/2.6	10	2	268 × 480	300 × 380
EPI–DWI (b = 50, 400 and 800 s/mm2)	9400	70	90°	5	202 × 256	300 × 380
SWI	41.8	25.0	20°	5	216 × 368	280 × 380
DCE	3.7	1.7	15°	2	280 × 400	280 × 380

FSE: fast spin echo, GRE: gradient echo, EPI: echo planar imaging, DWI: diffusion-weighted imaging, SWI: susceptibility-weighted imaging, DCE: dynamic contrast-enhanced (repeated 6 times (duration 45 s each) after intravenous administration of 0.1 mmol/kg Gd-DTPA (Magnevist; Bayer, Berlin, Germany) at 2 mL/s (followed by a flush of 20-mL saline solution) via a power injector with a 15-second timing delay

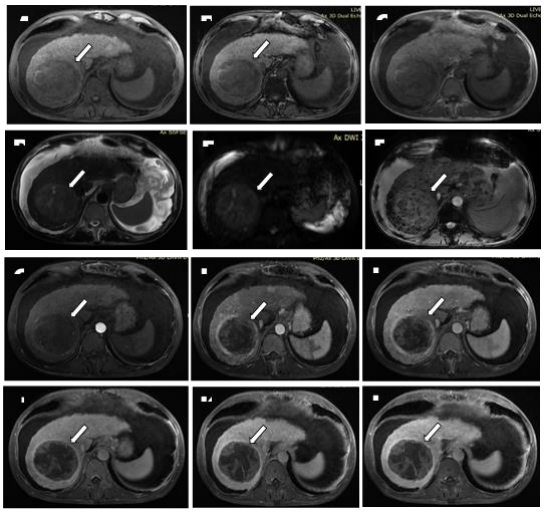

Figure 1. Case of cirrhosis positive HCC (LIRADS 5) 88×86 mm with six significant imaging findings in a 61-year-old man with chronic viral hepatitis B. (A) Ax T1 weighted imaging hypo density mass (arrow). (B-C) Ax 3D Dual echo single drop mass (arrow). (D) Ax T2 weighted imaging mass mild to moderate (arrow). (E) Ax Diffusion-weighted imaging (b=800 sec/mm2) The mass shows diffusion restriction with high SI (arrow) (F) Ax SWI group B (hyperintensity with background sidrosis) (arrow). (G-L) Ax Dynamic contrast-enhanced (DCE) arterial phase image shows heterogeneous arterial mass enhancement (arrow), and the central low SI area is in segment VII of the liver and pseudo-capsule no washout in the portal phase (arrow)

Results

Clinical and imaging characteristics

Between October 2023 and March 2024, a total of 43 cases suspected of HCC were initially considered for inclusion in this study. However, after excluding patients diagnosed with other types of liver cancer, those who had received pre-operative treatment, those with poor image quality, and those lacking necessary pathological results, a final cohort of 43 cases were included (27 males [62.8%] and 16 females [37.2%], with a median age of 53.0 years).

The diagnostic efficacy of different MRI sequences in distinguishing HCC from benign liver nodules was assessed using receiver operating characteristic (ROC) curve analysis. The area under the curve (AUC), sensitivity, and specificity were calculated for each sequence, revealing varying levels of diagnostic performance.

T1-weighted imaging

The 3D AXI GRE T1 sequence demonstrated an AUC of 0.692, with a sensitivity of 92.3% and a specificity of 40% at a cut-off value of 0.5. The Ax 3D Dual Echo BH sequence had a slightly lower AUC of 0.612, with the same sensitivity (92.3%) but reduced specificity (30%) (Figure 2).

T2-weighted imaging

The Ax SSFSE BH sequence showed a stronger diagnostic performance with an AUC of 0.801, sensitivity of 92.3%, and specificity of 66.7% at a cut-off value of 1.5 (Figure 3).

Diffusion-weighted imaging (DWI)

The ADC values derived from DWI sequences exhibited limited diagnostic accuracy, with an AUC of 0.512, sensitivity of 92.3%, and specificity of 96.3% at a cut-off value of 0.5 (Figure 4).

Dynamic contrast-enhanced MRI (DCE-MRI)

Among the DCE-MRI sequences, the arterial phase demonstrated the highest diagnostic accuracy with an AUC of 1.00, achieving 100% sensitivity and specificity at a cut-off value of 1.5. The venous phase had an AUC of 0.608, with sensitivity and specificity of 96.7% and 23.1%, respectively, at a cut-off of 5.5. The delayed phase showed an AUC of 0.771, with a sensitivity of 96.7% and specificity of 53.8% at a cut-off value of 1.5 (Figure 5).

The DCE-MRI arterial phase outperformed other sequences, providing perfect diagnostic accuracy (AUC=1.00) in distinguishing HCC from benign lesions. T2-weighted imaging also showed strong diagnostic potential, while the DWI sequences, particularly ADC values, displayed limited efficacy in this context (Table 2).

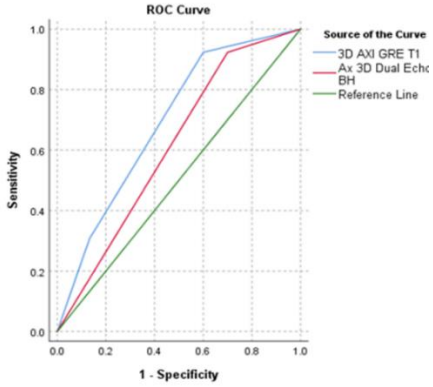

Figure 2. ROC curve of T1-weighted Imaging in Differentiating HCC from Benign Lesions

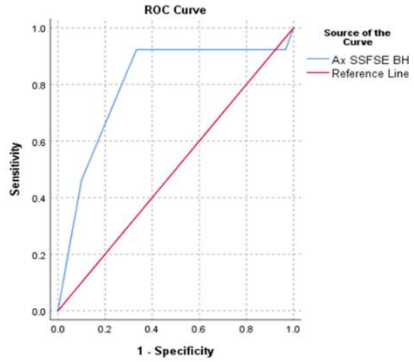

Figure 3. ROC curve of T2-weighted Imaging in Differentiating HCC from Benign Lesions

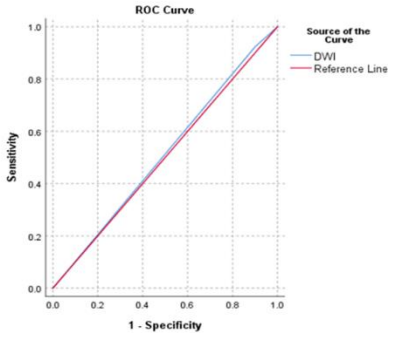

Figure 4. ROC curve of DWI in Differentiating HCC from Benign Lesions

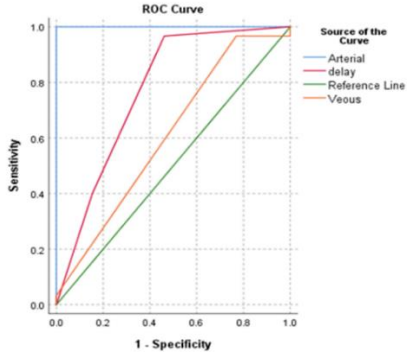

Figure 5. ROC curve of DCE-MRI Phases in Differentiating HCC from Benign Lesions

Table 2. Diagnostic performance of MRI sequences in differentiating HCC from benign liver lesions

		Sensitivity	Specificity	AUC	Cut-off
T1	**3D AXI GRE T1**	92.3%	40%	0.692 (0.528-0.857)	0.5
	Ax 3D Dual Echo BH	92.3%	30%	0.612(0.437-0.786)	0.5
T2	**Ax SSFSE BH**	92.3%	66.7%	0.801 (0.644-0.959)	1.5
ADC		92.3%	96.3%	0.512 (0.323-0.700)	0.5
DCE	**Arterial**	100%	100%	1.00 (1.00-1.00)	1.5
	Venous	96.7%	23.1%	0.608(0.416-0.800)	5.5
	Delay	96.7%	53.8%	0.771 (0.598-0.943)	1.5

Discussion

Accurately classifying liver nodules as benign and HCC is crucial for effective management strategies, such as surveillance or biopsy. LI-RADS has been developed to standardize the reporting and management of liver nodules detected in imaging studies, including DCE-MRI (11). Despite the advantages of LI-RADS, its ability to differentiate benign nodules from (HCC)can be complex, particularly in cases where radiologist uncertainty or disagreement is present. Studies have reported limitations in accurately classifying nodules within the LR-3, LR-4, and LR-5 categories using this system. Consequently, LR-3 lesions often require repeat imaging every six months until a definitive diagnosis is reached, while biopsy is typically recommended for most LR-4 nodules (12). Therefore, this approach needs to be evaluated to determine whether it accurately predicts the type of tumor without contributing to artificial errors.

We performed a recent study concerned with LI-RADS-v2018 major imaging features. We revealed excellent interobserver agreement for LR-1, LR-2, LR-5, and LR-TIV, with good agreement for LR-3 and LR-4 and excellent inter-observer agreement for the major imaging features (13). So, in the current study, we focused on both ADC and DCE analysis; the ADC and DCE were used to differentiate and classification of hepatocellular carcinoma and benign liver nodules with Sensitivity and Specificity of ADC 92.3% and 96.0%, respectively, and with Sensitivity and Specificity of arterial DCE 98% and 99% respectively.

Prior studies were designed to assess the value of DWI. They measured ADC values in a selected group of hepatic focal lesions mainly concerned with differentiating between benign and malignant lesions. A prospective recent study evaluated the value of DWI in improving the sensitivity of LI-RADS classification of small hepatic lesions (≤20 mm), which were formerly characterized as LI-RADS grade 3-5 on dynamic contrast-enhanced CT (14), unlike our study, in which we included all variable LI-RADS v2018 categories. One retrospective study evaluated the performance of DWI and T2-weighted imaging in the detection of HCC about the LI-RADS version 2014 with only LI-RADS grade 3-5 lesions (15), while in our study, we included all LI-RADS categories and LI-RADS major imaging features as the reference standard.

A recent study used ADC values to differentiate between haemangioma and HCC, where ADC values of haemangiomas were significantly higher than those of HCC (16). Another recent study stated that quantitative ADC histogram analysis increases the accuracy of the diagnosis of HCC compared to other primary liver cancers, and the combination of quantitative ADC measurement and LI-RADS improves this distinction (17).

Like any study, the present study has some limitations. First, the study included only 43 patients, which is relatively small for a diagnostic accuracy study. This limited sample size might reduce the generalizability of the findings and could lead to potential biases in the results. Second, this study was conducted in a single center, which may limit the applicability of the findings to other settings. Variations in imaging protocols, equipment, and radiologist expertise across different centers could affect the reproducibility of the results. Third, the follow-up period was limited to 12 months to confirm the benign nature of the lesions. Longer follow-up periods may be necessary to ensure no malignant transformation occurs in lesions initially classified as benign.

In summary, these results underscore the superior diagnostic accuracy of DCE-MRI in enhancing the LI-RADS system's ability to classify liver lesions, reinforcing its role in clinical practice. However, the study also highlights the need for further investigation into the role of ADC values and other imaging modalities in complementing and refining the diagnostic process.

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