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Research Article

DIAGNOSTIC UTILITY OF DIFFUSION-WEIGHTED IMAGING AND APPARENT DIFFUSION COEFFICIENT IN DIFFERENTIATING BENIGN AND MALIGNANT FOCAL LIVER LESIONS: A CROSS-SECTIONAL STUDY

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ABSTRACT

The liver is a common site for various focal liver lesions (FLLs), ranging from benign conditions to malignant tumors. Accurate differentiation between benign and malignant FLLs is crucial for effective patient management. This study evaluates the role of diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) values in characterizing FLLs. Conducted in the Department of Radio-Diagnosis at Sri Lakshmi Narayana Institute of Medical Sciences, Pondichery, India, over a two-year period, this cross-sectional study analyzed 94 patients diagnosed with FLLs through ultrasonography (USG), multi-detector computed tomography (MDCT), and magnetic resonance imaging (MRI). DWI, a non-invasive MRI technique, leverages differences in water proton mobility to differentiate between tissue types. This study found that all malignant FLLs (n=39) exhibited true diffusion restriction on DWI and lower ADC values (mean: $1.0155 \pm 0.147 \times 10^{-3}$ mm²/s) compared to benign lesions (mean: $2.1952 \pm 0.308 \times 10^{-3}$ mm²/s). The ADC value ranges for malignant and benign lesions (excluding abscesses) were 0.8-1.3 $\times 10^{-3}$ mm²/s and 1.5-3.5 $\times 10^{-3}$ mm²/s, respectively. Notably, hepatic abscesses, despite being benign, also showed restricted diffusion with overlapping ADC values (mean: 0.9×10^{-3} mm²/s), necessitating additional clinical and imaging evaluation to distinguish them from malignant lesions. This study underscores the utility of DWI and ADC mapping as effective tools in differentiating benign from malignant FLLs, particularly when contrast agents are contraindicated. DWI, combined with conventional MRI sequences, can significantly reduce the need for invasive procedures like biopsies. The findings suggest that DWI should be integrated into routine liver imaging protocols for its high diagnostic accuracy.

Keywords: - Focal liver lesions, diffusion-weighted imaging, apparent diffusion coefficient, MRI, liver cancer, hepatic abscess, diagnostic imaging, non-invasive diagnosis.

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INTRODUCTION

The liver, a vital organ in the human body, is often the site of various benign or malignant, primary or secondary focal liver lesions (FLLs). FLLs are abnormal areas of tissue within the liver that may manifest as solid or cystic masses. The term "lesion" is preferred over "mass" in this context because "lesion" encompasses a broader range of abnormalities, including both solid and cystic forms. These lesions can range from solitary benign conditions to multiple metastases originating from primary tumors elsewhere in the body. With the advancement of imaging modalities, the detection and characterization of FLLs

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have significantly improved, leading to better diagnosis and management of liver diseases [1].

The development and widespread use of advanced imaging techniques such as ultrasonography (USG), triple-phase computed tomography (CT) scans, and magnetic resonance imaging (MRI) have increased the rate of detection of FLLs [2]. Among these modalities, MRI has emerged as a particularly valuable tool for the assessment and characterization of focal hepatic lesions. The introduction of faster MRI sequences has enabled high-quality imaging of the entire liver, providing excellent intrinsic soft tissue contrast. Unlike CT scans, MRI does not involve ionizing radiation, making it a safer option for repeated imaging. Additionally, the use of gadolinium-enhanced multiphasic imaging with high temporal and spatial resolution, coupled with fat suppression techniques, has made MRI the most accurate modality for characterizing liver lesions [3].

A key advantage of MRI in the evaluation of FLLs is the use of diffusion-weighted imaging (DWI) sequences. DWI is an MRI technique that derives its image contrast from differences in the mobility of protons, primarily associated with water, between tissues. In highly cellular tissues, such as tumors, the extracellular space is more tortuous, and the density of hydrophobic cellular membranes is higher, which restricts the apparent diffusion of water protons [4]. DWI was initially developed for neuroimaging applications, such as detecting acute cerebral strokes and assessing demyelinating diseases and intracranial tumors [5]. However, with advancements in imaging technology, DWI has become increasingly valuable in liver imaging as well [6].

DWI measurements are relatively quick, typically taking only 1-5 minutes, and do not require the administration of exogenous contrast agents. This makes DWI a convenient addition to existing imaging protocols without significantly increasing examination time. Moreover, DWI provides both qualitative and quantitative information that can be helpful in assessing tumors [7]. The quantitative measure derived from DWI is known as the apparent diffusion coefficient (ADC), which reflects the molecular mobility of water molecules within tissues. The ADC value depends on factors such as extracellular space, viscosity, and cellularity. Several studies have demonstrated the utility of ADC in differentiating between benign and malignant hepatic lesions [8].

In particular, a reduction in the mean ADC value (indicated by low signal intensity on an ADC map) is often associated with malignancy in FLLs. However, ADC values can vary between studies, partly due to differences in equipment and b-values used in the imaging process [9]. Despite these variations, the combination of DWI and ADC measurement has proven to be an important method for the in vivo quantification of the combined effects of capillary perfusion and diffusion. As a result, DWI has become an essential component of MRI protocols for assessing FLLs, particularly in distinguishing between benign and malignant lesions [10].

In conclusion, MRI, with its superior soft tissue contrast and non-ionizing nature, has become the imaging modality of choice for characterizing FLLs. The addition of DWI sequences enhances its diagnostic accuracy, providing valuable information on tumor cellularity and treatment response. As imaging technology continues to advance, the role of DWI in liver imaging is expected to grow, offering more precise and reliable assessments of focal liver lesions.

Aims and Objectives

1. **To determine the role of diffusion-weighted MR imaging in differentiating between benign and malignant hepatic lesions by calculating apparent diffusion coefficient (ADC) values.**
   Diffusion-weighted MR imaging (DWI) has gained prominence as a non-invasive diagnostic tool for liver lesions. The primary aim of this study is to evaluate its effectiveness in distinguishing between benign and malignant hepatic lesions by analyzing ADC values. By quantifying the diffusion of water molecules within tissues, ADC measurements provide insights into cellular density, which can aid in identifying malignant characteristics in liver lesions.
2. **To provide a quantitative cut-off range of ADC values to differentiate between benign and malignant lesions.**
   Establishing a quantitative threshold for ADC values is critical for improving diagnostic accuracy. This study seeks to define a specific range of ADC values that can reliably differentiate between benign and malignant liver lesions, potentially serving as a valuable reference for clinical practice.

MATERIALS AND METHODS

The study was conducted in the Department of Radio-Diagnosis at Sri Lakshmi Narayana Institute of Medical Sciences, Pondichery, India, over a period of two years, from September 2017 to September 2019. The study was designed as a cross-sectional analytical study, with data collected and analyzed from a diverse group of patients presenting with focal liver lesions. The methodology is outlined below:

Study Design:

This study was a cross-sectional analytical study conducted over one year. It focused on evaluating

patients diagnosed with focal liver lesions using various imaging techniques.

Source of Data:

The data for this study were obtained from patients diagnosed with focal liver lesions using ultrasonography (USG), multi-detector computed tomography (MDCT), and magnetic resonance imaging (MRI) of the abdomen and pelvis at P.B.M. Hospital, Bikaner.

Sample Size:

A total of 94 patients who met the inclusion criteria were included in the study. The sample size was initially calculated using Buderer's formula, which estimated a required sample size of 30 cases based on anticipated sensitivity, specificity, and prevalence. However, due to a higher number of eligible patients during the study period, a total of 94 cases were analyzed.

Selection Criteria:

Inclusion Criteria:

- Patients undergoing multimodality evaluation in the department and found to have focal liver lesions.
- Patients with diagnosed focal liver lesions confirmed through histopathology, LIRADS (Liver Imaging Reporting and Data System), or biochemical methods.
- Patients of all age groups.

Exclusion Criteria:

- Patients with metallic implants, cardiac pacemakers, or cochlear implants.
- Patients who are claustrophobic or unwilling to undergo imaging.
- Patients with hepatic neoplasms who have undergone chemotherapy or radiation therapy.

METHODS:

Data Collection:

Patients who met the inclusion criteria were enrolled in the study and administered a predesigned, pretested pro forma (Annexure II). Demographic characteristics such as age and sex were obtained through an interview. The patients were also briefed on the procedure, including the noise produced by gradient coils and the importance of remaining still during the imaging process.

Imaging Protocol:

Patients diagnosed with liver lesions underwent diffusion-weighted MR imaging (DWI) using a 3 Tesla MRI scanner at P.B.M. Hospital, Bikaner. The imaging parameters were as follows:

- Field of View (FOV): 350 to 400 mm in adults, 180 to 200 mm in pediatric patients.
- Slice Thickness: 4 to 5 mm.
- Matrix Size: 512 x 512 pixels.
- Sequences Obtained: Spin-echo T1-weighted (axial/coronal), spin-echo T2-weighted (axial/coronal), axial and coronal FIESTA, and single-shot echo-planar imaging (axial) for DWI.

Diffusion MR Imaging:

DWI was performed using single-shot echo-planar imaging (EPI) with b-values of 50, 500, and 1000 sec/mm². ADC values were calculated by marking three regions of interest (ROI) within the liver lesions. The mean ADC values were then calculated and compared with results from USG, contrast-enhanced CT scans, and histopathology or other laboratory investigations as available.

Statistical Analysis:

The data collected during the study were coded and entered into a Microsoft Excel worksheet. Categorical data were expressed as rates, ratios, proportions, and percentages, while continuous data were presented as mean ± standard deviation. Statistical tests were conducted with significance set at a p-value of ≤ 0.05.

RESULTS:

Categorical data, such as demographic characteristics and lesion types, were expressed as rates, ratios, proportions, and percentages. [11] Continuous data, including ADC values, were summarized using mean ± standard deviation (SD). For statistical analysis, the ANOVA test and unpaired t-test were employed to compare means between groups.[12] A p-value of 0.05 or less was considered statistically significant. In this prospective study, a total of 94 patients with focal liver lesions (FLLs) were included. Of these, 68.1% (64 patients) were male, and 31.9% (30 patients) were female. The age of the participants ranged from 21 to 80 years, with the majority falling within the 51-60 year age group, which comprised 29 patients. The mean age of the study population was 53 years.[13]

The focal liver lesions included in the study encompassed a variety of pathologies, such as hemangiomas, abscesses, hepatic cysts, hydatid cysts, hepatocellular carcinomas (HCC), and metastases. Among these, hepatocellular carcinoma was the most common lesion, accounting for 26 cases, followed by hemangioma with 21 cases, and hepatic cysts with 15 cases.[14] Other lesions included metastases (13 cases), abscesses (10 cases), and hydatid cysts (9 cases). In terms of age distribution for specific lesions, hemangiomas

were more commonly observed in the 41-50 year age group, hepatic cysts in the 51-60 year age group, abscesses in the 31-40 year age group, hydatid cysts in the 51-60 year age group, metastases in the 31-40 year age group, and HCC in the 51-60 year age group. Out of the 94 patients studied, 55 were found to have benign lesions, while 39 had malignant lesions. [15] Among the FLLs, all malignant lesions, such as hepatocellular carcinomas and metastases, exhibited diffusion restriction on diffusion-weighted imaging (DWI). Conversely, benign lesions, including hepatic cysts, hydatid cysts, and hemangiomas, generally showed high signal intensity on both DWI and ADC maps. The exception to this pattern was hepatic abscesses, which, despite being benign, also exhibited diffusion restriction. [16]

Apparent diffusion coefficient (ADC) values were calculated for all focal liver lesions. The malignant lesions that exhibited diffusion restriction, specifically hepatocellular carcinomas and metastases, had mean ADC values of 0.98 ± 0.16 x 10^{-3} mm^2/sec and 1.04 ± 0.12 x 10^{-3} mm^2/sec, respectively. The range of ADC values for HCC was between 0.8 and 1.2 x 10^{-3} mm^2/sec, while for metastases, it ranged from 0.8 to 1.3 x 10^{-3} mm^2/sec. Notably, abscesses, despite being benign, also showed diffusion restriction, with a mean ADC value of 0.92 ± 0.05 x 10^{-3} mm^2/sec and a range of 0.6 to 1.1 x 10^{-3} mm^2/sec. For other benign lesions, such as hepatic cysts, hydatid cysts, and hemangiomas, the mean ADC values were significantly higher, reflecting their benign nature. The mean ADC values were 2.95 ± 0.42 x 10^{-3} mm^2/sec for hepatic cysts, 3.05 ± 0.30 x 10^{-3} mm^2/sec for hydatid cysts, and 1.84 ± 0.31 x 10^{-3} mm^2/sec for hemangiomas.[17] The overall mean ADC values for benign and malignant FLLs were calculated as 2.1952 ± 0.30 x 10^{-3} mm^2/sec for benign lesions and 1.015 ± 0.14 x 10^{-3} mm^2/sec for malignant lesions. The ADC values for benign FLLs (excluding abscesses) ranged from 1.5 to 3.5 x 10^{-3} mm^2/sec, while the ADC values for malignant lesions ranged from 0.8 to 1.3 x 10^{-3} mm^2/sec. These findings highlight the potential of ADC values as a quantitative tool for differentiating between benign and malignant focal liver lesions. [18].

Figure 1: a) and b) DWI image showing well defined lesion which is showing diffusion restriction with ADC values of 0.61 x 10-3mm2 / sec. d) the lesion shows high signal intensity in T2WI. Case of hepatic abscess.

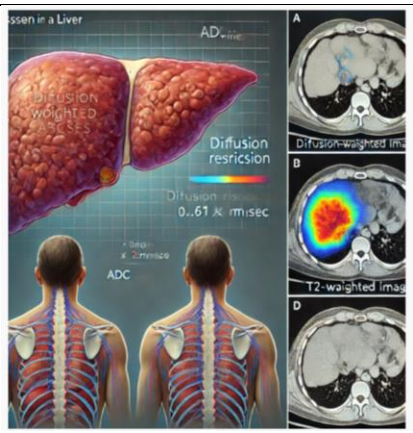


Figure 2: a) T2 WI shows well defined hyperintense lesion with hypointense ring shaped structure within it. b), c) and d) DWI image with ADC shows no restriction of lesion with ADC values of 3.1 x 10-3mm2 / sec. Case of hydatid cyst.

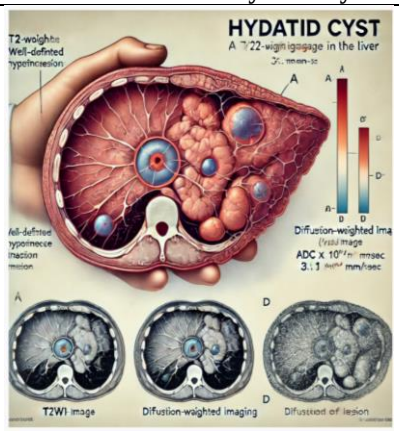
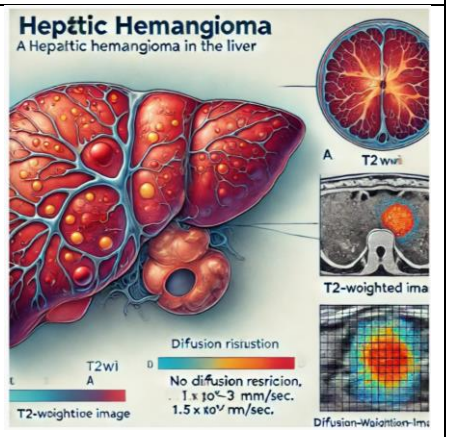


Figure 3: a) T2 WI showing well defined hyperintense lesion. b), c) and d) DWI image showing no diffusion restriction with ADC value of 1.5 x 10-3mm2 / sec. Case of hepatic hemangioma.



DISCUSSION AND CONCLUSION

1. **Characterization of Liver Lesions:** Based on both qualitative and quantitative assessments using Diffusion-Weighted Imaging (DWI) and Apparent Diffusion Coefficient (ADC) maps, different liver lesions were effectively characterized. DWI facilitated the differentiation between benign and malignant lesions, making it a valuable diagnostic tool, especially in patients where contrast agents are contraindicated (e.g., those with renal impairment).[19-20] The need for Fine-Needle Aspiration Cytology (FNAC) or biopsy in differentiating between benign and malignant lesions can be potentially reduced through the use of DWI. However, DWI should always be interpreted alongside conventional MRI sequences due to potential overlap in ADC values between different liver lesions. [21-23]

2. **Recommended ADC Value Ranges:** The study suggests using the ADC value ranges of 1.5 to 3.5 × 10^{-3} mm^2/s for benign lesions (excluding abscesses) and 0.8 to 1.3 × 10^{-3} mm^2/s for malignant lesions. These ranges can assist in differentiating benign from malignant focal liver lesions (FLLs).
3. **Exception for Hepatic Abscesses:** Hepatic abscesses presented lower ADC values, with a mean of 0.9 × 10^{-3} mm^2/s, which overlaps with the ADC values of malignant FLLs. In such cases, clinical evaluation and classical imaging features from MRI and CT scans are essential for distinguishing abscesses from malignant FLLs.[24-25]
4. **Screening and Diagnostic Utility of DWI:** DWI, combined with ADC, can be effectively used as a screening tool for detecting FLLs and as a diagnostic tool for characterizing them as benign or malignant. It is recommended to perform DWI at both low and high b-values (0, 500, and 1000) to achieve high sensitivity in detecting FLLs.
5. **Study Outcomes:** In a cohort of 94 patients with focal hepatic lesions screened using DWI, the following key outcomes were observed:
    - **Malignant FLLs (n=39):** All malignant FLLs demonstrated true diffusion restriction on DWI and ADC maps.
    - **Benign FLLs (n=55):** Out of 55 benign FLLs, 45 showed high signal intensity on both DWI and ADC maps, while 10 benign FLLs, which were abscesses, showed restricted diffusion on DWI and ADC maps.
    - **Biopsy Confirmation:** Of the 39 lesions classified as malignant based on imaging findings using MDCT and USG, 26 underwent biopsy, all of which confirmed malignancy.
    - **ADC Values:** Malignant FLLs exhibited lower ADC values compared to benign FLLs, with the mean ADC values for benign and malignant lesions being 2.1952 ± 0.308 × 10^{-3} mm^2/s and 1.0155 ± 0.147 × 10^{-3} mm^2/s, respectively.
    - **ADC Value Ranges:** The ADC values for malignant FLLs ranged from 0.8 × 10^{-3} mm^2/s to 1.3 × 10^{-3} mm^2/s, while for benign FLLs (excluding abscesses), the range was 1.5 × 10^{-3} to 3.5 × 10^{-3} mm^2/s.
    - **Differentiation of Lesions:** Using these ADC value ranges, benign lesions (except abscesses) were differentiated from malignant lesions.
    - **Abscesses with Restricted Diffusion:** The 10 benign cases that showed restricted diffusion were identified as abscesses, which had lower ADC values (mean of 0.9 × 10^{-3} mm^2/s), overlapping with the ADC values of malignant FLLs. In these scenarios, additional clinical and imaging features from MRI and CT were necessary to distinguish abscesses from malignant FLLs.

In conclusion, DWI and ADC mapping provide valuable insights in the detection and characterization of focal liver lesions, serving as reliable tools in differentiating between benign and malignant lesion.

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