

Differentiation Between Hepatic Hemangioma and Metastasis by Diffusion Weighted MRI

Ahmed Mohamed Helmy*, Mahmoud Abdel Latif, Amina Ahmed Sultan

Department of Diagnostic Radiology, Faculty of Medicine, Mansoura University, Egypt

*Corresponding author: Ahmed Mohamed Helmy El Diasty, Mobile: (+20) 01067705006,

E-Mail: ahmedabouhelmy@gmail.com

ABSTRACT

Background: Diagnosis of hepatic focal lesions could be done by magnetic resonance imaging (MRI) study especially when diffusion-weighted magnetic resonance imaging (DWI) is included in the imaging protocol with apparent diffusion coefficient (ADC) quantification. Several studies have demonstrated that combining DWI with ADC measurement plays an important role in the detection and characterization of hepatic focal lesions and differentiating hemangioma from hepatic deposits.

Objective: The current study aimed at evaluation of the role of diffusion weighted imaging differentiating between hepatic hemangioma and metastasis (1-4 lesions in number) by diffusion weighted MRI in patient pathologically proved to have primary malignancy.

Patient and methods: Fifty cases were included; patients referred to Radiology Department of Mansoura University Hospital. There were 33 females and 17 male patients with age ranged from 26 to 82 years. All patients were subjected to proper history taking and DWI MRI. This study was using a 1.5 T Philips Ingenia MRI scanner.

Results: ADC had significantly lower values in patients with metastatic hepatic lesions with mean ADC 0.93 (SD 0.21) $\times 10^{-3}$ mm²/sec. ADC had significantly higher values in patients with hemangioma with mean ADC 1.96 (SD 0.31) $\times 10^{-3}$ mm²/sec. The mean ADC value in the metastatic group was statistically significantly lower compared to the hemangioma group. ADC had sensitivity and specificity of 100 % and 95.8% respectively, and an accuracy of 97.4% in differentiating between hemangioma and metastasis cases, when a cut-off value of 1.55 $\times 10^{-3}$ mm²/s was applied.

Conclusion: Combined qualitative and quantitative analysis of DWI and ADC values respectively can help in differentiation between hepatic hemangioma and metastatic deposits. Using DWI and ADC in conjunction with conventional imaging found to be a simple and non-invasive tool that aid in differentiation between hepatic hemangioma and metastatic deposits.

Keywords: Diffusion weighted imaging, Apparent diffusion coefficient, MRI, Hepatic hemangioma, Hepatic metastasis.

INTRODUCTION

With an incidence of up to 20% of the population, hepatic hemangiomas are not only the most frequent benign liver lesion but also the most frequent primary hepatic tumors overall. With a female-to-male ratio that can approach 5:1⁽¹⁾.

One of the organs that is most frequently affected by metastatic disease is the liver. Primary liver tumors are 18 to 40 times less frequent than secondary lesions. Because of its abundant blood supply, the liver serves as a favorable "soil" for the spread of metastatic disease⁽²⁾. Magnetic resonance imaging (MRI) is a non-invasive imaging technique that has superior soft tissue contrasts and potential physiological and functional application. Due to its superior contrast resolution and lack of ionizing radiation, MRI is frequently used to diagnose liver lesions⁽³⁾.

Diffusion-weighted magnetic resonance imaging (DWI) is integrated into the routine liver imaging protocol. DWI plays an emerging role for the assessment of focal and diffuse liver diseases⁽⁴⁾.

A non-invasive imaging method with superior soft tissue contrasts and potential physiological and functional applications is magnetic resonance imaging (MRI). MRI is commonly used to diagnose liver abnormalities due to its higher contrast resolution and lack of ionizing radiation⁽³⁾.

The standard liver imaging protocol includes DWI. For the assessment of localized and diffuse liver disorders, DWI is becoming more important⁽⁴⁾.

The aim of the current study was to evaluate the role of diffusion weighted imaging differentiating between hepatic hemangioma and metastasis (1-4 lesions in number) by diffusion weighted MRI in patient pathologically proved to have primary malignancy.

PATIENT AND METHODS

A total of 50 cases were included; patients referred from General Surgery Department and Oncology Centre Mansoura University (OCMU) with clinical or radiological proven to have primary malignant tumour with hepatic focal lesions (1-4 in number) suspected to be hepatic haemangioma or metastatic during the period from December 2019 to July 2022.

There were 33 females and 17 male patients with age ranged from 26 to 82 years. All patients were subjected to proper history taking and DWI MRI.

Inclusion criteria:

- Patients who agreed to participate in study.
- Patients already diagnosed with primary malignancy and present with hepatic focal lesion (1-4 in number) detected by

radiological studies and suspected to be hepatic hemangioma or metastases.

- Cases who were diagnosed comfortably upon clinical evaluation, laboratory studies and or follow-up radiological examinations

Exclusion criteria:

Patient not suitable for MRI examination have been excluded:

- Patients who have a cardiac pacemaker.
- Patients who have metallic foreign body.
- Patients with severe claustrophobia to MRI device.
- Patients with very bad general condition.
- Uncooperative patients.

Methodology:

Magnetic Resonance Imaging:

All cases in this study were processed using the Philips Ingenia 1.5 T MRI scanner located in the Radiology Department of Mansoura University Hospital (with the same scanning parameters).

I. Patient preparation:

Patients were instructed to avoid movement during the acquisition time. Before entering the examination room, the patient was instructed to remove all metallic objects and all clothes containing metal. Irritable patients were reassured and informed about the examination. No sedation was used in any of the examinations. The patients were informed of the examination time as well as the importance of remaining motionless during the examination.

II. Technique:

The patient lied supine, head first on the MRI table and a surface coil was used. Scanning was performed from the lung bases to the iliac crest.

III. T2 weighted pulse sequences:

Axial T2-weighted image (1250/80) TR/TE with an 18 cm field of view, 256 x 256 matrix, 2 mm section thickness, and 1 mm section gap made up the first imaging.

IV. Diffusion weighted MRI:

Utilizing single shot spin echo planar imaging (SS-EPI) in the axial plane, diffusion weighted images were produced. Diffusion was produced using the following parameters: slice thickness = 5 mm; interslice gap = 1 mm; FOV = 25 cm; repetition time (TR) 2745 ms; echo time (TE) 75 ms; matrix, 256 256; acquisition time = 50 sec. ' In the axial plane, three b-factors of 0, 500, and 1000 mm²/sec were achieved.

Image analysis:

The abnormal regions on DW MRI and apparent diffusion coefficient (ADC) map were outlined by using the conventional images as a guide and Regions of

interest (ROI's) are drawn manually on the ADC map for quantitative analysis.

Signal characteristics on DWI and ADC maps: hyperintense for bright and as a hypointense for those with low signal intensity compared to normal liver tissue.

We assessed whether the lesion shows diffusion restriction or non-restricted. We defined lesion as visually restricted if it appeared hyperintense at diffusion sequence with low signal intensity on the corresponding extracted ADC map image relative to the surrounding normal parenchyma.

ADC calculation:

Measurements of ADC were made by putting the cursor on the ADC map in different ROIs. The ADC values were expressed in 10⁻³ mm²/sec. ROIs were defined as slightly smaller than the liver metastases and hemangiomas in order to reduce partial volume effects

Regions of interest (ROI) for each lesion were placed not less than three times. Then the average ADC value was calculated. In cystic necrotic lesions ADCs were measured in the wall and solid parts.

Ethical consent:

This study was ethically approved by the Institutional Review Board of the Faculty of Medicine, Mansoura University. Written informed consent was taken from all participants. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). The Kolmogorov-Smirnov test was used to determine whether the data were normal. The Unpaired Student-t test was used to compare normally distributed continuous data, which are reported as mean (SD). Number-based nominal data were analyzed using the Chi-square test (percentage). When necessary, data are presented graphically. P value ≤0.05 was considered significant.

RESULTS

According to the diffusion results, this table shows that the mean ADC value in the haemangioma group was 1.96 (SD 0.31) x10⁻³ mm²/s and the mean ADC in the metastatic group was 0.93 (SD 0.21) x10⁻³ mm²/s. The mean ADC value in the metastatic group was statistically significantly lower compared to the haemangioma group (P value <0.001*) (**Table 1 and Figure 1**).

Table (1): Analysis of the ADC value in the two study groups:

Variable	Groups		Test of significance	P-value
	Hemangioma group (n = 24)	Metastatic group (n = 26)		
ADC x 10 ⁻³ mm ² /s	1.96 ± 0.31	0.93 ± 0.21	t = 13.847	<0.001*

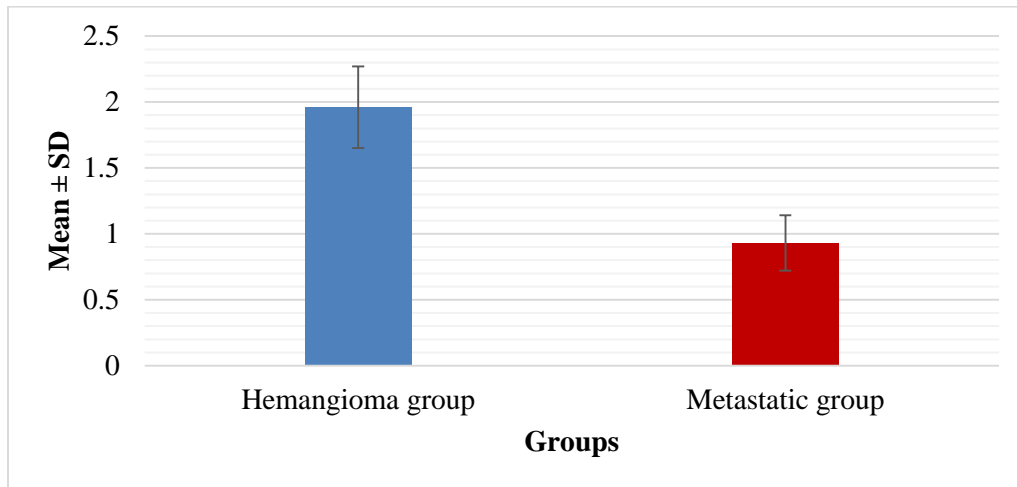


Figure (1): ADC value in the two study groups.

Table 2 shows that the best cutoff point of ADC value was 1.55 x10⁻³ mm²/s with 100% sensitivity, 95.8% specificity and total accuracy of 97.4% (Table 2 and Figure 2).

Table (2): Validity of ADC in differentiating malignant from benign lesions:

Variable	AUC (95%CI)	Cut off point	P value	Specificity %	Sensitivity %	NPV %	PPV %	Accuracy %
ADC (x10 ⁻³ mm ² /s)	0.997	1.55	<0.001*	95.8	100	100	96.2	97.4

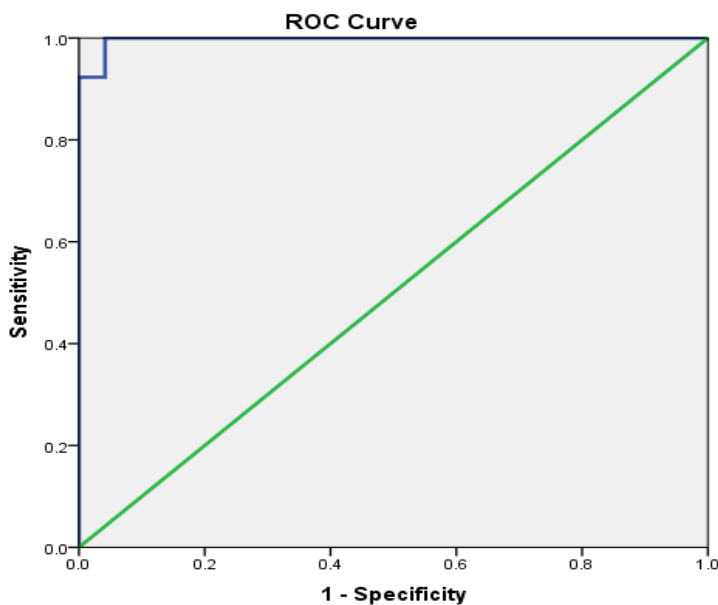
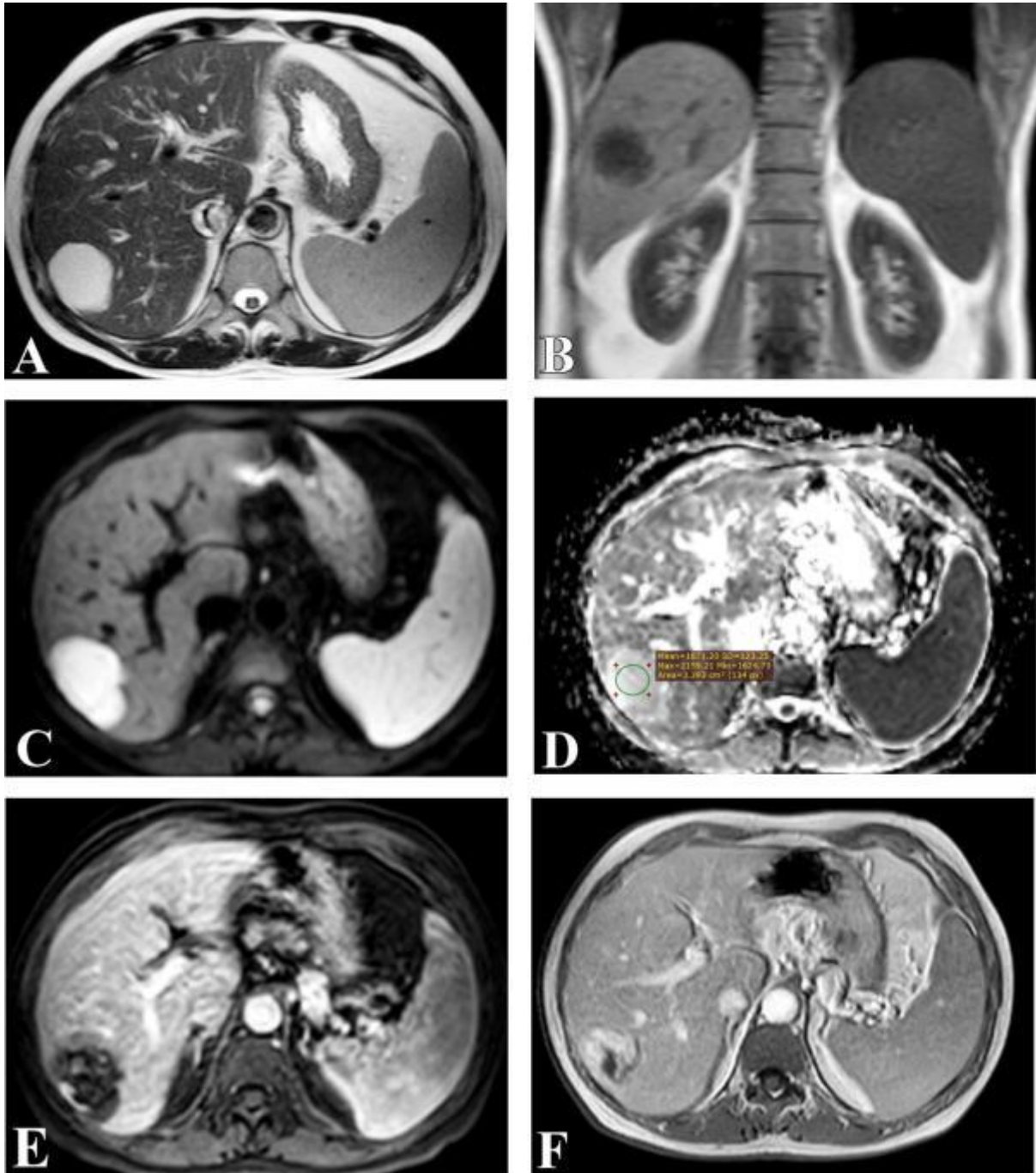
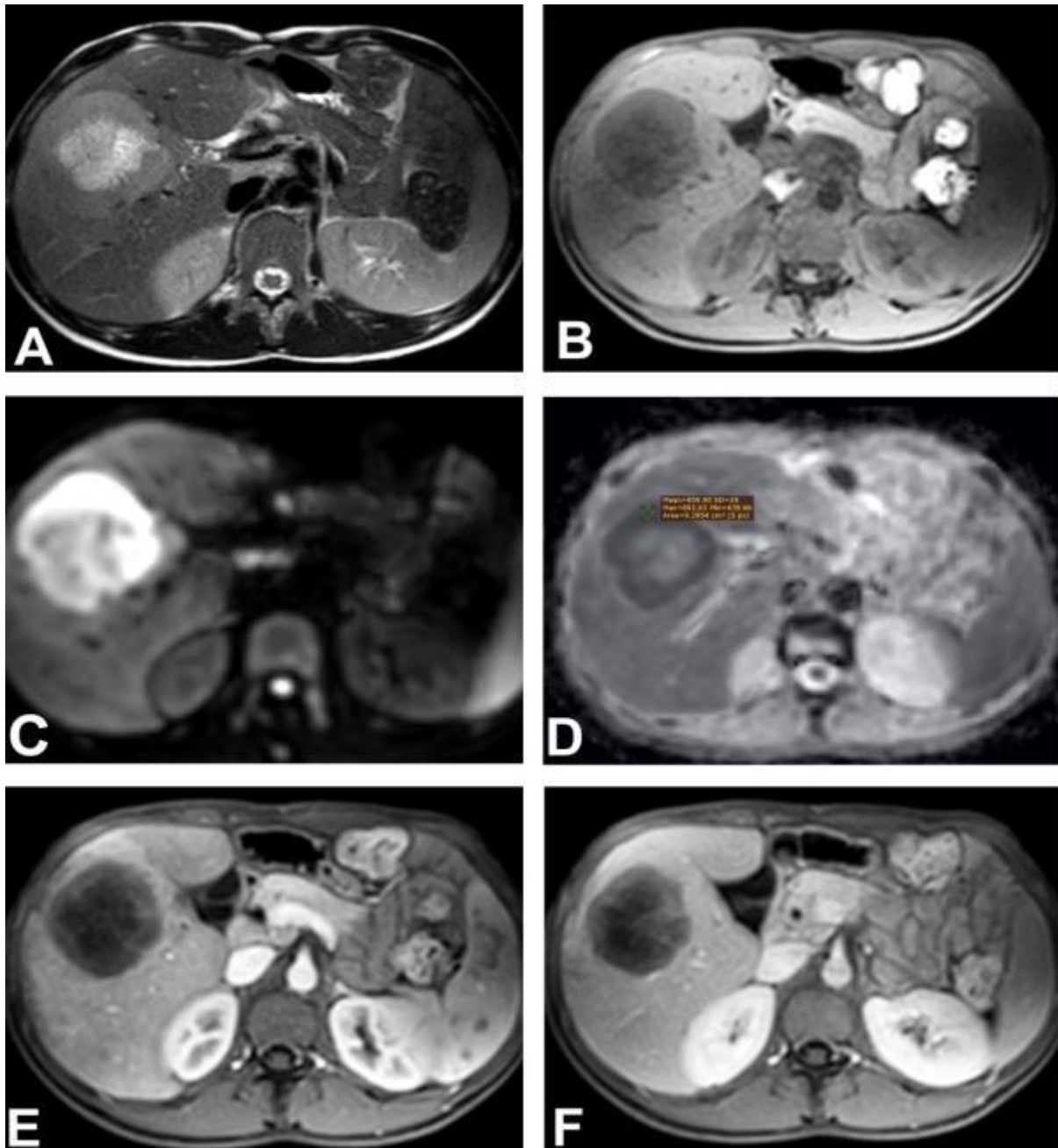


Figure (2): ROC curve of Using ADC to distinguish between hepatic hemangioma and metastasis.

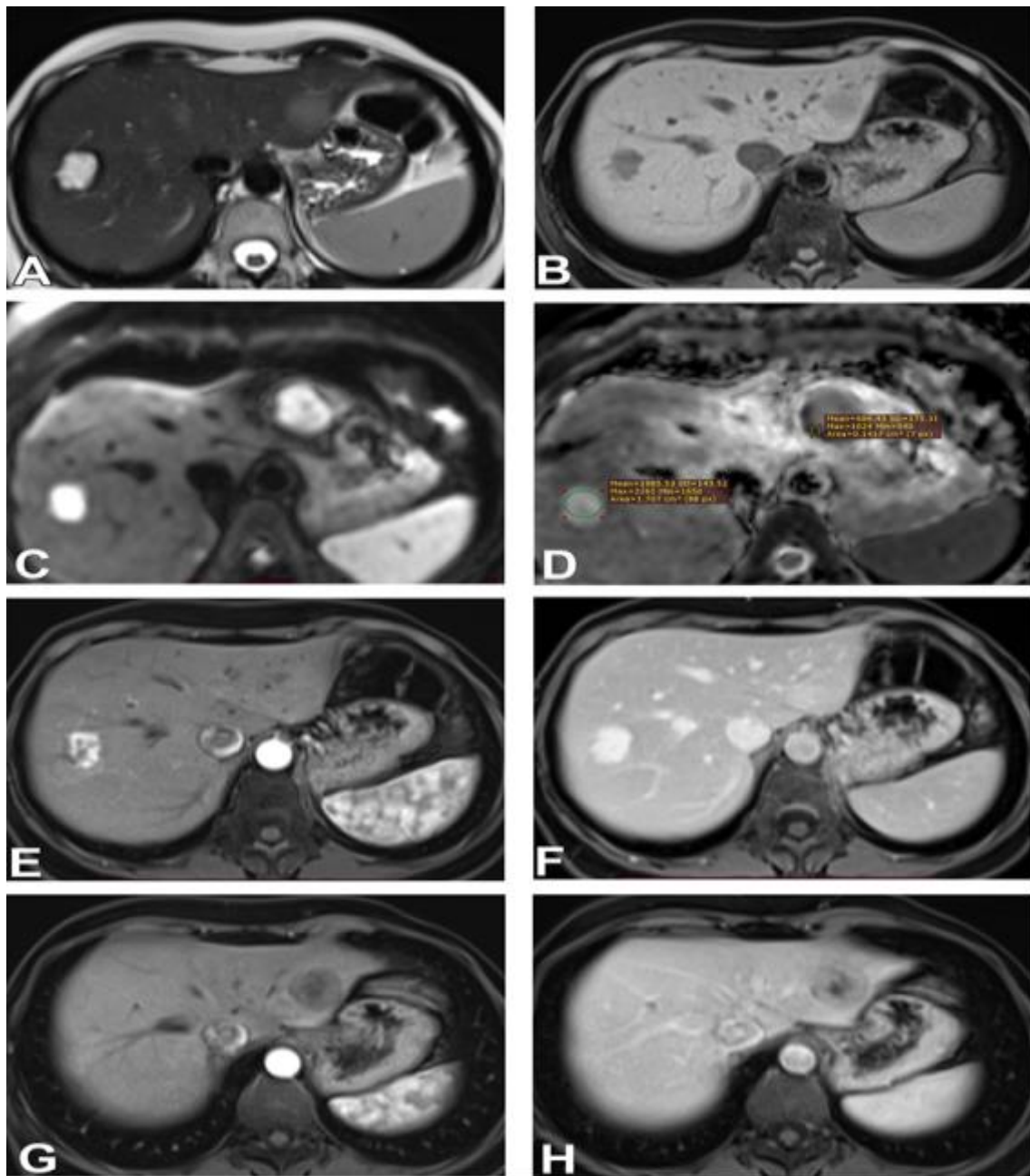
CASES PRESENTATION



Case (1): 62-year old male proved to have colon cancer with accidentally finding hepatic focal lesion. (A) Axial T2-WI shows hepatic focal lesion seen at segment VII displays high signal. (B) Axial T1-WI shows hepatic focal lesion seen at segment VII displaying low signal. (C) Axial DWI shows focal lesion displaying high SI (due to T2 shine through) (D) Axial ADC map shows focal lesion displaying high SI with the calculated mADC value equal to 1.87×10^{-3} s/mm² (free diffusion). (E) Arterial phase shows focal lesion showing peripheral nodular enhancement. (F) Delayed phase shows the focal lesion showing progressive centripetal filling enhancement
Final diagnosis: Hepatic hemangioma.



Case (2): 55-year old male proved to have pancreatic cancer presented with upper abdominal pain. (A) Axial T2-WI shows hepatic focal lesion seen at segment VI displays high signal. (B) Axial T1-WI shows hepatic focal lesion seen at segment VI displaying low signal. (C) Axial DWI shows focal lesion displaying high SI (D) Axial ADC map shows focal lesion displaying low SI peripherally with high central regions with the calculated mADC value of restricted part equal to 0.65×10^{-3} s/mm² (restricted diffusion). (E) Arterial phase shows focal lesion showing peripheral ring enhancement. (F) Portal phase shows the focal lesion showing peripheral ring enhancement. Final diagnosis: Metastatic poorly differentiated adenocarcinoma of pancreatic origin.



Case (3): 59-year old female proved to have breast cancer presented for metastatic work up. (A) Axial T2-WI shows two hepatic focal lesions segments VII and II display high signal. (B) Axial T1-WI shows two hepatic focal lesions seen at segments VII and II displaying low signal. (C) Axial DWI two hepatic focal lesions segments VII and II display high signal (D) Axial ADC map shows first focal lesion seen at segment II displaying low SI with the calculated mADC value equal to 0.68×10^{-3} s/mm² (restricted diffusion) and The other focal lesion seen at segment VII displays high SI with the calculated mADC value equal to 1.9×10^{-3} s/mm² (free diffusion). (E) and (G) Arterial phase shows the first focal lesion showing peripheral ring enhancement and the second focal lesion showing peripheral nodular enhancement. (F) and (H) Delayed phase shows the first focal lesion showing peripheral ring enhancement and the second focal lesion showing progressive centripetal filling.

- Final diagnosis: First HFL: Metastatic adenocarcinoma of breast origin.
- Second HFL: Hepatic hemangioma.

DISCUSSION

When evaluating liver lesions, MRI is frequently used as a problem-solving method. Functional imaging and anatomic and morphologic evaluation are both possible with MRI. For the identification and characterization of liver metastases, non-enhanced MRI sequences are necessary⁽⁵⁾.

The random motion of water molecules in the tissues is measured by DWI. The diffusion coefficient depends on the rate of diffusion. The apparent diffusion coefficient (ADC) is employed in clinical practice to assess diffusion since the diffusion coefficient can be impacted by the tissue's temperature, microcirculation, perfusion, magnetic susceptibility, or any form of movement⁽⁶⁾.

It can occasionally be challenging to distinguish between a hemangioma and a metastasis using standard MRI sequences. Hemangiomas and metastases can typically be distinguished from one another on contrast-enhanced images by the presence of a typical enhancement pattern. Smaller than 2 cm hemangiomas may exhibit homogeneous enhancement and be confusing. DWI is beneficial in this situation⁽⁷⁾.

The level of permeability and interstitial free fluid are connected to the diffusion characteristics of tissues. On the whole, cancer tissues show higher diffusion restriction. The liver tumor foci exhibit reduced ADC values and limited diffusion on DWI⁽⁸⁾. The normal structure of tissues is distorted in cancerous tissues. This inhibits the water's macromolecular mobility, restricting diffusion in cases of cancer, and lowers the measured ADC⁽⁹⁾.

In the current study, all hepatic metastatic lesions showed increased signal intensity on DWI and low signal on ADC maps. For necrotic lesions, the wall showed low signal on ADC maps, while all hemangiomas showed increased signal intensity on DWI images and high signal on ADC maps.

In accordance with our findings, **Testa et al.**⁽¹⁰⁾, **Caraianni et al.**⁽¹¹⁾, and **Tokgoz et al.**⁽¹²⁾, reported that benign focal liver lesions (i.e. hemangiomas) demonstrated high SI in both DWI and ADC map. Whereas **Kele and van der Jagt**⁽¹³⁾, **Roldán-Valadez et al.**⁽¹⁴⁾ and **Gluskin et al.**⁽¹⁵⁾ reported that malignant solid tumors (i.e. metastases) demonstrated high SI in DWI and low SI on the ADC map.

The rising use of DWI MRI has been impeded by problems like technical restrictions and challenges. The hyper-intensity of tissue with normal diffusion in DW imaging is referred to as the T2 shine effect, which is caused by a lengthy T2 decay time. The intrinsic characteristics of the lesions being imaged, such as cellular composition, lesion size, and even the anatomical location of the lesion, might affect the T2 shine effect⁽¹⁶⁾. This impact is particularly notable in diseases like hemangiomas where DW imaging may mislead towards hyper-cellular lesions, including malignant lesions⁽¹⁷⁾.

In the current study, the mean ADC value in the hemangioma group was 1.96 (SD 0.31) $\times 10^{-3}$ mm²/s and the mean ADC in the metastatic group was 0.93 (SD 0.21) $\times 10^{-3}$ mm²/s. The mean ADC value in the metastatic group was statistically significantly lower compared to the haemangioma group.

The study by **Omer et al.**⁽¹⁸⁾, which comprised 30 cases of hemangiomas and 47 cases of metastases, revealed that there was a substantial statistical difference between the mean ADC values for the two types of lesions: 0.83 $\times 10^{-3}$ mm²/s for metastases and 2.1 $\times 10^{-3}$ mm²/s for hemangiomas. It was statistically significant (P <0.001) that benign and malignant lesions had different mean ADC values.

According to **El-Refaei et al.**⁽¹⁹⁾, there was a very statistically significant distinction between hemangioma and metastases in terms of mean ADC (P <0.001). In the hemangioma group, the mean ADC value was 2.11 $\times 10^{-3}$ mm²/s, but in the metastatic group, it was 1.34 $\times 10^{-3}$ mm²/s.

According to **Javadrashid et al.**⁽²⁰⁾, there was a highly statistically significant difference between the mean ADC values of the haemangioma (1.6134 $\times 10^{-3}$ mm²/s) and the metastatic lesion (0.8451 $\times 10^{-3}$ mm²/s). In benign lesions, the ADC value was substantially higher (P <0.001).

Additionally, **Sivrioglu and Kafadar**⁽²¹⁾ demonstrated that metastases measured 0.79 (SD 0.14) mm²/s and haemangiomas measured 1.58 (SD 0.23) mm²/s.

The current study shows that the best cutoff point of ADC value was 1.55 $\times 10^{-3}$ mm²/s with 100% sensitivity, 95.8% specificity and total accuracy of 97.4%.

Filipe et al.⁽²²⁾ determined that the ADC value of malignant lesions is much lower compared to benign lesions after using the cut-off value of 1.43 $\times 10^{-3}$ mm²/s to distinguish benign from malignant lesions.

Ergelen et al.⁽²³⁾ reported that hemangiomas and metastatic masses differed statistically significantly. With a threshold ADC value of 1.33 $\times 10^{-3}$ mm²/s, lesions could be distinguished with a sensitivity and specificity of 81% and 86%, respectively, according to ROC analysis (P <0.001).

Tokgoz et al.⁽¹²⁾ demonstrated using ROC curve analysis that the "cut-off" ADC value of 1.800103 mm²/s had a sensitivity of 97.4% and a specificity of 90.9% for differentiating hemangioma from malignant liver lesions.

The use of varied hardware, the lack of standardization in picture capture (option of different b values), multiple methodologies for ADC calculation, and distinct patient demographics are a few probable explanations for the variance in ADC and cut off values⁽²⁴⁾.

Sivrioglu and Kafadar⁽²¹⁾ made the assumption that the ROI measuring method may have contributed to these disparities.

In the current study, although there was a statistically significant difference in the mean mADC values of hemangioma and metastasis, there was slight overlap in mADC values between hemangioma and metastases, two hyper vascular metastatic lesions were detected with relatively high mADC measuring about $1.45 \times 10^{-3} \text{ mm}^2/\text{s}$ and $1.49 \times 10^{-3} \text{ mm}^2/\text{s}$.

This is in line with **Kim et al.** (25) findings' that it can be challenging to distinguish between hemangiomas and metastases. DWI sequences and ADC maps can be used to tell these lesions apart from one another. When these lesions were differentiated, there were similar ADC values. This might be because hemangiomas and hypervascular metastases both exhibit hypervascular features.

Despite the current findings, this study has some limitations including the small sample size and being a single center study. Also, the study didn't include benign lesions other than hemangioma or malignant lesions other than metastases. Also the complete cystic metastases were excluded from this study as may lead to differences in ADC measurements. This could be considered in further studies.

In conclusion, combined qualitative and quantitative analysis of DWI and ADC values respectively can help in differentiation between hepatic hemangioma and metastatic deposits. Using DWI and ADC in conjunction with conventional imaging found to be a simple and non-invasive tool that aid in differentiation between hepatic hemangioma and metastatic deposits. In cases with contraindication to contrast administration DWI and ADC can be used as an alternative technique to contrast-enhanced imaging.

Financial support and sponsorship: Nil.

Conflict of interest: Nil.

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