Original paper

# Role of ADC Value in Differentiation of Malignant and Benign Hepatic Lesion.

**Choman Sabah Omer [1*], Kawa A. Mahmood[2], Rezheen Jamal Rashid[1]**

[1] *Department of Radiology, Sulaimani Teaching hospital, Sulaymaniyah, Ministry of Health, Kurdistan region, Iraq.*
[2] *Department of Surgery, Diagnostic Imaging Unit, Sulaimani College of Medicine, University of Sulaimani, Sulaymaniyah, Kurdistan Region Iraq.*

## Abstract

**Background:** Apparent diffusion coefficient ADC value used in this research for differentiation of the malignant and benign hepatic lesions, which has an impact on the management of these lesions by surgery or conservatively.
**Aim:** To analyze the role of diffusion weighted imaging (DWI) with the apparent diffusion coefficient (ADC) values in the differentiation of malignant from benign hepatic lesions.
**Materials and methods:** this is a prospective cross-sectional study 80 patients with 118 focal hepatic lesions contributed. MRI with DWI examination was carried out for all patients. After DWI examination, an ADC map was created and ADC values were measured for 118 focal hepatic lesions.
**Results:** out of 118 hepatic lesions, 62 were benign and 56 were malignant. Benign lesions comprised 30 hemangiomas and 21 simple cysts, 6 focal nodular hyperplasia (FNH), 4 abscesses and 1 adenoma. Malignant lesions comprised 47 metastases, 6 hepatocellular carcinomas (HCC), 2 fibrolamellar hepatocellular carcinomas and 1 case intra hepatic cholangiocarcinoma. The highest ADC values were measured for cysts. The mean ADC value of benign lesions was $2.27 \pm 0.7 \times 10^{-3}$mm²/sec, whereas malignant lesions had a mean ADC value of $0.85 \pm 0.18 \times 10^{-3}$mm²/sec. The mean ADC value of benign lesions was significantly higher than that of malignant lesions ($P < 0.001$).
**Conclusion:** DWI and quantitative measurement of ADC values shows promising result in characterization of benign and malignant hepatic lesions, with other MRI sequences of dynamic contrast study. Especially, when contrast is contraindicated.
**Key words:** Magnetic resonance imaging MRI, Diffusion Weighted Imaging DWI, Apparent Diffusion Coefficient (ADC) value, hepatic lesions.

## Introduction

Liver lesions can be detected by different imaging modalities like Ultrasound (US), computed tomography (CT) and Magnetic resonance imaging (MRI). MRI has a major contribution in the diagnosis of focal liver lesions [(1)].
MRI is superior through assessing morphology and signal intensity in different MR sequences and showing pattern of enhancement with dynamic contrast study, in addition to the absence of ionizing radiation hazards and iodinated contrast drawbacks [(1, 2)].
Since 1990s diffusion weighted imaging (DWI) has had been used in the early time of the detection of the brain ischemic changes and central nervous system (CNS) pathology like tumors and demyelinating diseases. Now DWI is one of the standard sequences in the hepatic MRI protocol for focal hepatic lesions [(3)].
With advancing MR sequences and availability of echo planar imaging, Quality of abdominal MRI dramatically improved, especially dynamic liver MRI. Images with

*for correspondence email: chomansabah@gmail.com

better spatial resolution and subsequent more accurate, noninvasive detection and characterization of hepatic lesions, these achieved by stronger magnetic field, more powerful gradients, and more sensitive receiver coils [4-7].

Diffusion is a physical phenomenon of random microscopic movement of water molecules. It is known to be a sensitive parameter in microscopic tissue characterization and predict cellular density of lesions. Currently, it is possible to determine diffusion by measuring diffusion-weighted MRI and ADC value in vivo [8]. Diffusion-weighted imaging can be performed after strong bipolar pulses are added to spin echo or gradient echo sequences, by sensitizing the water in tissue to diffusion. Thus, the freely mobile and restricted viscous water molecules can be evaluated, and balance of intracellular and extracellular compartment water can be seen [9].

Diffusion-weighted MRI examinations have many technical difficulties, because it's very sensitive for movement such as physiologic activity like respiratory, cardiac, or peristaltic movements, all of which affect quality of the images and make evaluation more difficult. Fortunately, faster MRI technique can be achieved with the development of echo-planar imaging, which helps radiologists to overcome the long imaging times and related artifacts of conventional techniques [10, 11].

Acquisition of diffusion imaging potentially affected by different technical parameters, which are greatly reflecting on the ADC calculation such as the type of MRI equipment, parameters of the sequences, apnea or free breathing technique, the b values utilized and the number of different b values [12]. The b value represents strength of DWI, different b value help to quantify the apparent diffusion coefficient (ADC) [3].

Primary or secondary hepatic lesion detection and characterization are important part of management, particularly in those who need surgical intervention or chemotherapy. DWI can be used for this purpose, because it can give different tissue contrast without use of contrast, can be done before or after contrast without affecting image quality as gadolinium does not affect DWI and in a short breath hold time [13]. DW imaging is able to differentiate focal liver lesions with high water content (cysts and hemangioma) from solid lesions [14].

## Aim of study

To analyze the role of diffusion weighted imaging (DWI) with the apparent diffusion coefficient (ADC) values in the differentiation of malignant from benign hepatic lesions.

## Patients and methods

This prospective cross-sectional study included 80 patients with age range (23-84 years), having focal liver lesion by abdominal US or CT incidentally or as a surveillance for metastases in those with known primary malignancy.

Patient with poor quality DWI, those whom failed to maintain a breath hold or had a contraindication for MRI (like MR incompatible prosthesis or cardiac pacemaker), were excluded from study, as well as when diagnostic confirmation couldn't be achieved. The study approved by the ethical committee of KBMS and informed consent was obtained.

MRI protocol

Routine upper abdominal MRI examination was performed on (80) patients using a 1.5Tesla MRI device (Philips ACHIEVA 1.5 T) and (Siemens MAGNETOM Aera 1.5T). Standard examination composed of the following sequences:

Philips scanner have T2 TSE axial (TR/TE: 400/80ms), T2 SPAIR axial and coronal (TR/TE: 570/80ms), Dual in /out phase axial (in phase TR/TE:147/4.7, out phase TR/TE: 147/2.3ms), T1 e-Thrive axial and coronal (TR/TE: 4.9/1.8ms) unenhanced

with dynamic enhancement (25 sec, 60sec, 90 sec, 3min, 5min and 8min), DWI axial (TR/TE: 4278/262ms), while Siemens scanner had T2 haste coronal (TR/TE: 1000/89ms), T2 haste fat suppression axial (TR/TE:1000/93ms), Dual in /out phase axial (in phase TR/TE:6.8/4.8, out phase TR/TE: 6.8/2.4ms) T1 Vibe axial and coronal (TR/TE: 6.8/4.8ms) unenhanced with dynamic enhancement (25 sec, 60sec, 3min and 8min , DWI axial (TR/TE: 7100/64ms), contrast used was dimeglumine gadopentetate (Magnevist, Bayer) 0.1 mmole/Kg given manually or through a power injector at a rate of 2 mL/sec.

Diffusion weighted sequences in axial planes were obtained, single shot echo planer sequences in all 3 axes (x,y & z) by applying gradients ( in order to sensitize SE sequence to diffusion), and 2 different b values (b = 0 sec/mm² and b = 800 sec/mm²). The first series of the image set was composed of echo-planar spin echo T2-weighted images (b = 0 sec/mm²), the next 3 series of images were applied to the first series in x, y, and z axes (value of diffusion sensitizing gradients, b = 800 sec/mm²), and the last series of isotropic images were calculated from the projection of the diffusion vectors in all 3 axes.

The device automatically forms ADC maps from isotropic images and from those maps all mean ADC values of the lesions were measured. In order to measure ADC value, a circular region of interest (ROI) was used. For large lesions mean value of 3 different ROI measurements on the same slice were calculated. Also, in successive slices of same lesion a mean ADC value was determined by taking the mean of ADC measurements of each slice. For heterogeneous lesions with necrosis, measurements were performed from non-necrotic part which showed contrast enhancement in post-contrast images.

In our study we used cut off ADC value ($1.5\times10^{-3}$mm²/sec) between benign and malignant lesion.

**Patients**

Eighty Patients between 23-84 years old age (mean age 53 years), male to female ratio 0.6 (male31 and female 49) with a total of (118) hepatic lesions were included in this study, during 7 months from 1st November 2018 to 30th May 2019, in Shahid Hemn and Hiwa Hospitals. Clinical demography of patients with focal liver lesions shown in table 1.

**Statistical analysis**

The "IBM SPSS Statistics version 25" was used for the analysis of the data and both descriptive and inferential statistics were used. Furthermore, a P-values of ($\leq$0.05, and <0.001) were considered as statistically significant, and highly significant associations, respectively. In addition, Pearson Chi-Square was used to find out the significance of association between independent and dependent variable pairs, and Pearson's R Correlation was used to calculate the direction of the correlation between the two variables.

## Results

This study included 118 hepatic focal lesions in 80 patients, 21 case of simple hepatic cyst; 21(17.8%) cysts in 12 patients, which are diagnosed by typical imaging properties and follow up imaging studies, 30 (25.4%) hemangiomas of total 25 patients 8 of them proven by FNA , remaining of them proved by typical characteristic imaging features with serial follow up imaging studies, 4 (3.4%) abscess lesions in 3 cases diagnosed clinically and laboratory investigation with one of them aspirated, 5 cases (5.1%) of focal nodular hyperplasia (FNH) diagnosed by radiological feature and fine needle aspiration (FNA) in 3 cases, with largest one operated on. One case of adenoma (0.8%) diagnosed by typical imaging findings and clinically data, 2 cases fibrolamelar hepatocellular carcinoma (1.7%) diagnosed by excisional biopsy, 6 hepatocellular carcinoma (5.1%) in 5 cases

all of them in cirrhotic liver , 4 of them diagnosed by FNA other by imaging criteria, 1 case of intrahepatic cholangiocarcinoma (0.8%) diagnosed histopathologically through true cut biopsy, 47 cases of hepatic metastatic lesions (39.8%) in total 26 cases, with known primary malignancy 15 of them diagnosed by true cut biopsy, and 2 of them seen intra-operatively with excisional biopsy diagnosed as metastases and the remaining 9 cases have typical imaging characteristic of hepatic metastasis, these lesions with diagnostic confirmation by different tools showing in Table 2.

**Table 1.** clinical demography of patients with focal liver lesions.

| Variables | | Mean ± SD (Standard deviation) | Range |
|---|---|---|---|
| Age (year) | | 52.9 ± 14.7 | 23 to 84 |
| Age groups (year) (n=80) (%) | 20-29 | 4 (3.4) | |
| | 30-39 | 13 (11) | |
| | 40-49 | 21 (17.8) | |
| | 50-59 | 12 (10.2) | |
| | 60-69 | 19 (16.1) | |
| | 70-79 | 9 (7.6) | |
| | 80-89 | 2 (1.7) | |
| Gender (%) Male to female ratio = 0.6 | Female | 49 (61.25) | |
| | Male | 31 (38.75) | |
| | | | |
| Location of the lesions | | 62 right lobes/56 left lobes | |
| Size of lesions (cm) (n)(%) | <1 | 10 (9.4) | |
| | 1-3 | 73 (68.9) | |
| | 4-6 | 11 (10.4) | |
| | 7-9 | 5 (4.7) | |
| | 10-12.5 | 7 (6.6) | |
| Benign lesions n=62 (52.5%) | | Cyst n=21 (17.8%) | |
| | | Hemangioma n=30 (25.4%) | |
| | | FNH n=6 (5.1%) | |
| | | Adenoma n=1 (0.8%) | |
| | | Abscess n=4 (3.4%) | |
| Malignant lesions n=56 (47.5%) | | HCC n= 6 (5.1%) | |
| | | Fibrolamellar HCC n=2 (1.7%) | |
| | | Cholangiocarcinoma n=1 (0.8%) | |
| | | Metastases n=47 (39.8%) | |

**Table 2.** this table showing number of lesions with diagnostic confirmation by different tools.

| Lesions | Number of lesions | Diagnostic confirmation | |
|---|---|---|---|
| | | Radiological * | Histopathological** |
| Cyst | 21 (17.8%) | 21 | 0 |
| Hemangioma | 30 (25.4%) | 22 | 8 |
| Abscess | 4(3.4%) | 3 | 1 |
| FNH | 6 (5.1%) | 2 | 4 |
| Adenoma | 1 (0.8%) | 1 | 0 |
| Fibrolamellar HCC | 2 (1.7%) | 0 | 2 |
| HCC | 6 (5.1%) | 2 | 4 |
| Cholangiocarcinoma | 1 (0.8%) | 0 | 1 |
| Metastasis | 47 (39.8%) | 30 | 17 |
| Total | 118 (100.0%) | 81 | 37 |

*Radiological: typical imaging characteristic of specific focal hepatic liver lesion, or follow up scans with MRI or other imaging modalities.

*Histopathologically: tissue confirmation of the diagnosis through, aspiration, Fine Needle Aspiration (FNA), true cut biopsy or excisional biopsy.

The mean ADC value of the 62 benign lesions was 2.27 ± 0.7 x10 $^{-3}$mm$^2$/sec. ADC values of benign lesions were between 0.68 x10 $^{-3}$mm$^2$/sec and 3.4 x10 $^{-3}$mm$^2$/sec. The highest ADC value was for simple cysts, mean value 2.94 ± 0.33x10 $^{-3}$mm$^2$/sec. Among the benign lesions, pyogenic abscesses had the lowest ADC value, mean value 0.79 ± 0.13 x10 $^{-3}$mm$^2$/sec.

The ADC values of the 56 malignant lesions were between 0.4 x10 $^{-3}$mm$^2$/sec and 1.32 x10 $^{-3}$mm$^2$/sec, with a mean value of 0.85 ± 0.18 x10 $^{-3}$mm$^2$/sec. Among the malignant lesions, the lowest ADC value was for liver secondaries 0.83 ± 0.16 x10 $^{-3}$mm$^2$/sec, while cholangiocarcinoma had the highest value 1.32 x10 $^{-3}$mm$^2$/sec. There was a highly significant negative strong statistically significant association between ADC values and the diagnosis of liver diseases, the mean and range of ADC values of different lesions in our study shown on Table 3, and Fig 1 showing minimum and maximum value of ADC of hepatic lesions in a bar chart.

**Table 3. ADC values of focal liver lesions in our study**

| Liver lesions | Mean ± SD (x10 $^{-3}$3mm$^2$/sec) | Range |
|---|---|---|
| Secondary | 0.83 ± 0.16 | 0.4 to 1.11 |
| Cyst | 2.94 ± 0.33 | 2.12 to 3.40 |
| Fibrolamellar HCC | 1.02 ± 0.0071 | 1.01 to 1.02 |
| Hemangioma | 2.1 ± 0.42 | 1.48 to 3.30 |
| FNH | 1.65 ± 0.12 | 1.42 to 1.75 |
| HCC | 0.887 ± 0.22 | 0.49 to 1.09 |
| Cholangiocarcinoma | 1.32 ± (-) | 1.32 to 1.32 |
| Abscess | 0.79 ± 0.13 | 0.68 to 0.98 |
| Adenoma | 1.68 ± (-) | 1.68 to 1.68 |
| Benign | 2.27 ± 0.7 | 0.68 to 3.40 |
| Malignant | 0.85 ± 0.18 | 0.40 to 1.32 |

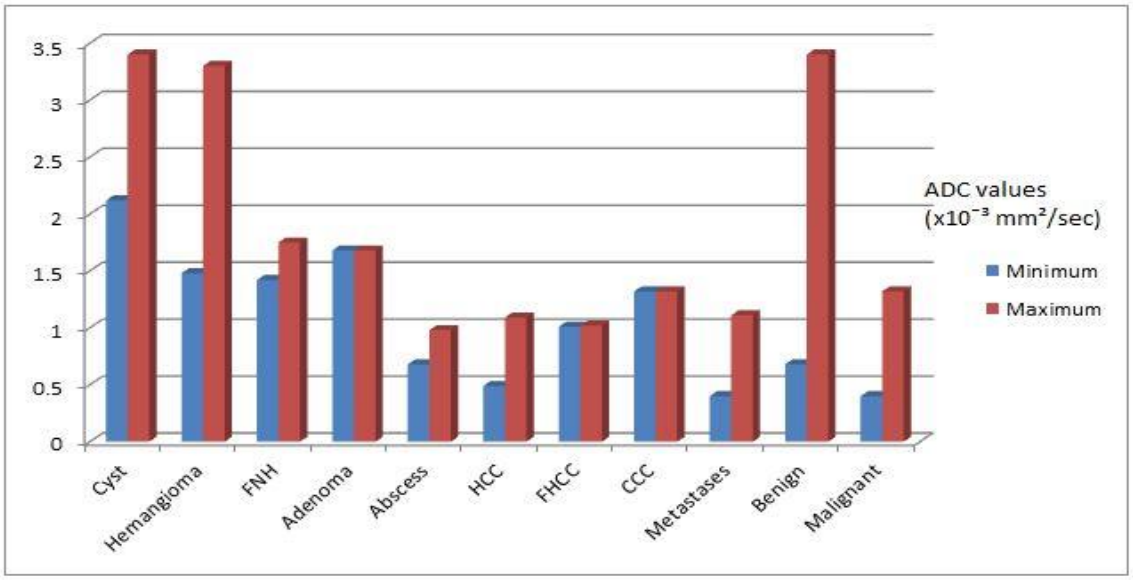


**Figure 1.** This bar chart showing ADC values of different focal liver lesions, benign lesions and malignant lesions in our study. FNH: focal nodular hyperplasia, HCC: hepatocellulaer carcinoma, FHCC fibrolamellar hepatocellular carcinoma, CCC: cholangiocarcinoma.

## Discussion

There is a broad differential diagnosis for focal liver lesions, great number of lesions show typical imaging characteristics, still diagnosing atypical lesions is challenging, need biopsy for accurate diagnosis. DWI has promising results in the characterization of typical lesions. Its advantages include less time for acquisition of images compared to routine MR sequences and contrast agents no require [14].

In our study highest ADC values for cysts (fig 2)and hemangioma (fig 3), their mean ADC value 2.94 ± 0.33×10 $^{-3}$mm²/sec and 2.1 ± 0.42 x10 $^{-3}$mm²/sec respectively , in comparison with previous studies our result near kim et al. 2.91×10 $^{-3}$mm²/sec and 2.04 – 2.10 x10 $^{-3}$mm²/sec [15], but its lower than result of Taouli et al 3.63×10 $^{-3}$mm²/sec and 2.95 x10 $^{-3}$mm²/sec [16], this difference might be related to the b value was used in these studies in our study and kim et al 800 sec/mm², while in Taouli <500 sec/mm² used.

Most authors utilize b values in the range of 500 to 800 sec/mm² for the evaluation of focal liver lesions; high b values underestimate the ADC because of the low signal to noise ratio (SNR) while low b values lead to an overestimation of the ADC because of the contribution of perfusion [12,17].

As mentioned by Ichikawa et al., b values were quite low (i.e., 1.6, 16, and 55 sec/mm²) and ADC values for abdominal organs were high [18]. They reported that when the b value is kept low, factors like perfusion and T2 time have greater relative effect on ADC measurements.

For same reason, they concluded that for abdominal diffusion studies, b values >400 sec/mm² might reflect ADC measurements more accurately [18]. However, again, Ichikawa et al. reported that higher b values cause lower quality on diffusion weighted images by low SNR and make evaluation harder [18].

Benign hepatocellular mass lesions (FNH and adenoma) were first evaluated by Taouli et al. and their ADC values were found to be lower than cysts and hemangiomas, and higher than malignant masses [16], similarly in our study they have lower ADC value than cyst and hemangioma and higher value than malignant lesions, mean ADC value of FNH 1.65 ± 0.12 x10$^{-3}$mm²/sec (fig:4) and for single case of hepatic adenoma 1.68 x10$^{-3}$mm²/sec.

The mean ADC value for the pyogenic abscess was very low in relative to other benign lesions 0.79 ± 0.13 x10 $^{-3}$mm²/sec, which is causing lower mean ADC value for whole benign lesions. This low ADC value could be related high viscosity of the content of the abscess. According to a study by Chan et al. on the use of MRI for the differentiation of abscesses and necrotic tumors [19], the mean ADC value was significantly lower for hepatic abscesses compared to necrotic tumors and simple cysts (0.67± 0.35 x10 $^{-3}$mm²/sec) (fig:5). Thus, the pyogenic abscess had a significantly lower ADC value compared to other benign lesions.

The lowest ADC values among the malignant masses in our study was belong to metastases mean value 0.83 ± 0.16 x10 $^{-3}$mm²/sec. This data is near result of Taouli et al.'s findings [16] which was 0.94 x10 $^{-3}$mm²/sec. while in Kim et al 1.06-1.11 x10 $^{-3}$mm²/sec even higher value in Parikh et al[20] and Miller et al.[21] reaching 1.5 x10 $^{-3}$mm²/sec, Miller , these difference might be related of type of primary malignancy and presence of large area of necrosis.

About HCC we have only 5 cases their mean ADC value was 0.887 ± 0.22 x10 $^{-3}$mm²/sec (fig: 6), which is near the finding of Namimoto et al[22] 0.99x10 $^{-3}$mm²/sec and much lower of than result of Taouli et al.[16] 1.33 x10 $^{-3}$mm²/sec, Miller et al[21] 1.54 x10 $^{-3}$mm²/sec, these difference explained by low b value used in two latter studies <500 sec²/mm, difference in size of necrotic areas in lesions.

We have only one case of Cholangiocarcinoma mean ADC value 1.32 x10 $^{-3}$mm²/sec, which has highest ADC value among malignant lesion in present study, which is lower than result in Yang, D. et al.[23] which was 1.52 x10 $^{-3}$mm²/sec and Namimoto et al 1.5 x10 $^{-3}$mm²/sec [22].
Over all Mean ADC value for all malignant lesions were 0.85 ± 0.18 x10 $^{-3}$mm²/sec, in other studies Kim et al[15] and Taouli et al[16] 1.01 and 1.08 x10 $^{-3}$mm²/sec respectively, these difference might be related to using different b value, which is more pronounced in Parikh and Miller 1.39 and 1.5 x $^{-3}$mm²/sec.[20,21]
While for benign lesions were 2.27 ± 0.7 x 10$^{-3}$mm²/sec , Kim et al 2.49, Taouli 2.45, Parikh et al 2.19 and miller 2.5 x $^{-3}$mm²/sec. our result for benign lesions lower than these studies might be related to presence of pyogenic abscess, which making lower mean ADC value, or related to large participation of simple hepatic cyst in other studies , they have free water mobility, give a very high ADC values, which is inversely highly affect the statistical analysis thus raising the ADC average on the benign lesions group.[15,16,20,21]
In our study, ADC measurements of benign and malignant hepatic lesions significantly different, which is similar to previous studies[16,18,22,24], the difference between the mean ADC values of benign and malignant lesions was statistically significant (P < 0.001) , but among the different benign lesions or among the different malignant lesions, there is no statistically significant differences in ADC values , these showing in the receiver operating characteristic (ROC) curve in fig:7, which supports similar previous findings where Onura et al. stated that the mean ADC values of malignant lesions were lower than benign lesions and these differences were statistically significant for all 3 diffusion gradients with P values of 0.0023, 0.0001, and < 0.01 while no statistically significant differences in ADC values among the different benign lesions or among the different malignant lesions[25].

## Conclusion

The ADC value is useful for the differentiation between benign and malignant focal liver lesions, in conjunction with other MR sequences, especially in those patients having contraindication of contrast.

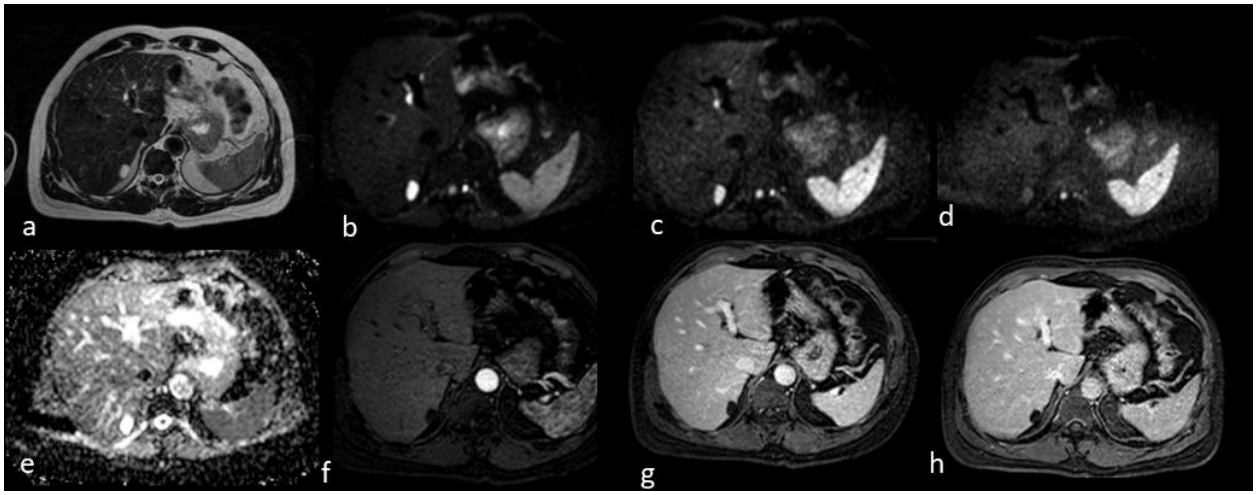


**Figure 2.** hepatic simple cyst, a.right lobe subcapsular small hepatic simple cyst in T2WI hyperintense signale , b. low b value of 50 sec/mm² , c. b value 400 sec/mm², d. loss of high signal intensity in high b value 800 sec/mm², e. hyperintense in ADC map showing high ADC value, f., g. and h. no enhancement after contrast application.

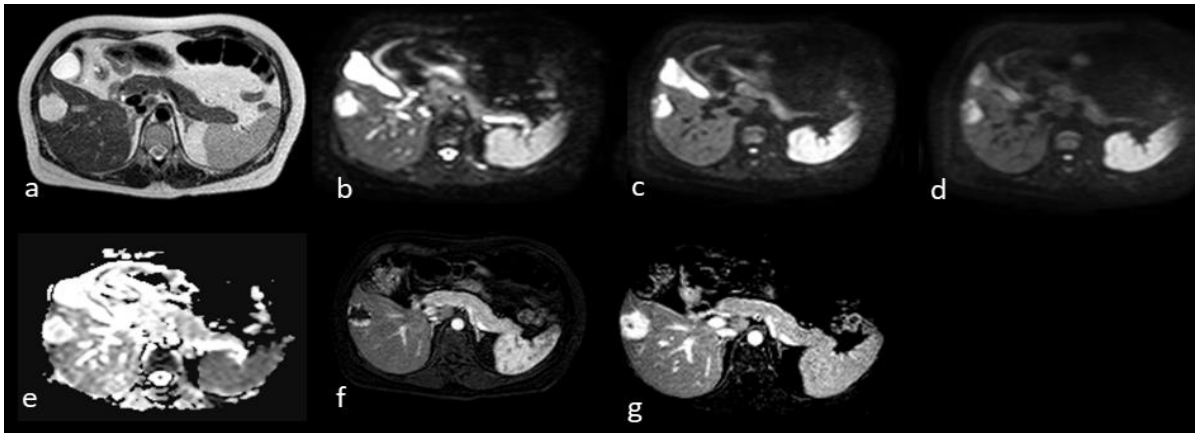


**Figure 4.** hepatic hemangioma, a. right hepatic lobe hyperintense lesion in T2WI, b. low b value of 50 sec/mm² hyperintense, c. b value 400 sec/mm² reduced intensity, d. high b value 800 sec/mm² more reduced intensity, e. hyperintense in ADC map showing high ADC value, f. early contrast, showed peripheral discontinuous nodular enhancement, g. late contrast more filling of the lesion with contrast.

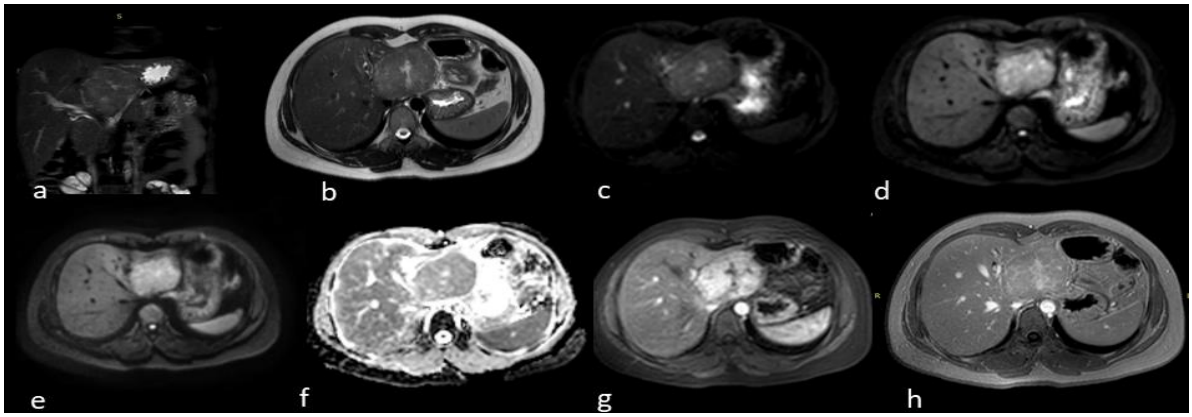


**Figure 4.** focal nodular hyperplasia , a. coronal T2WI with fat suppression b. axial T2WI left hepatic lobe slightly hyperintense lesion with hyperintense central scar , c. low b value of 50 sec/mm² hypointense, d. b value 400 sec/mm² increased intensity , e. high b value 800 sec/mm² more increased intensity , f. iso-intense in ADC map to liver parenchyma showing low ADC value, g. early contrast, showed avid homogenous enhancement , h. late contrast lesion become iso-intense with liver parenchyma and enhancement of the central scar with contrast .

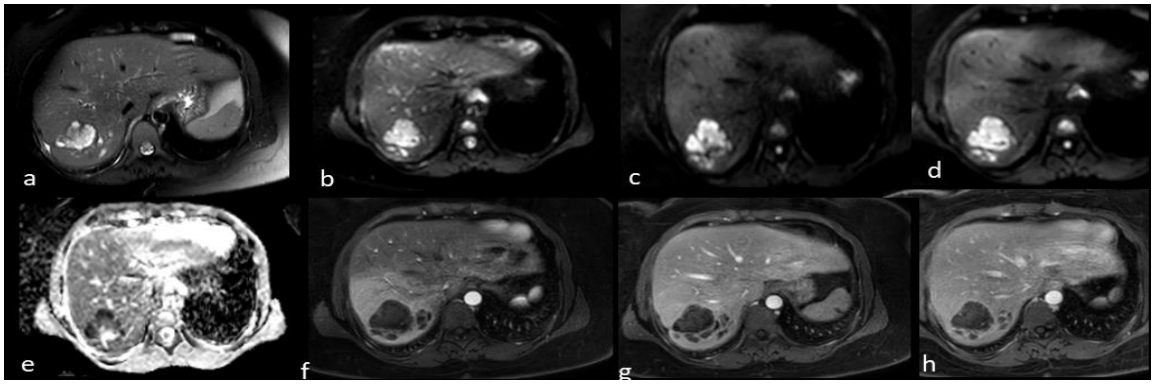


**Figure 5.** hepatic abscess, a. right hepatic lobe hyperintense lesion in T2WI, b. low b value of 50 sec/mm² hyperintense , c. b value 400 sec/mm² hyperintense, d. high b value 800 sec/mm² hyperintense , e. heterogeneous mostly hypointense in ADC map showing low ADC value, f. early contrast, showed peripheral ring enhancement with abnormal enhancement of surrounding liver parenchyma , g. and h. late contrast same ring enhancement with contrast .

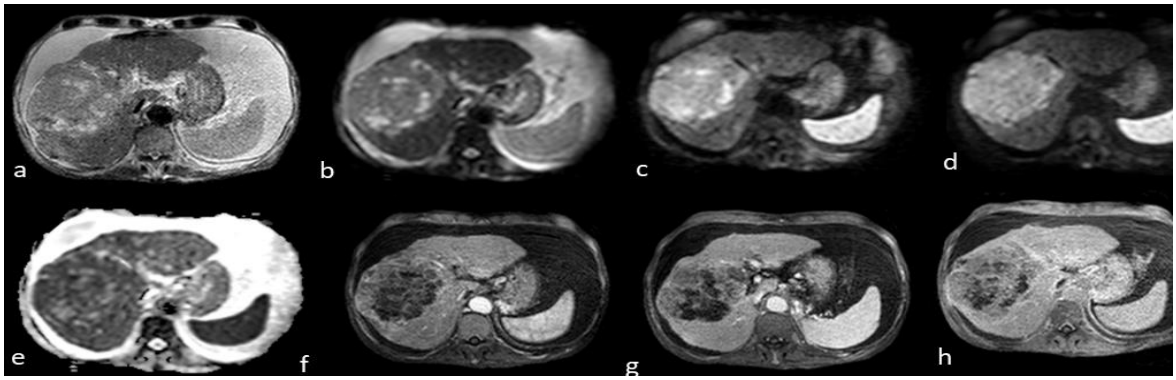


**Figure 6.** hepatocellular carcinoma , a. axial T2WI right hepatic lobe heterogeneous hyperintense lesion with hyperintense foci in the cirrhotic liver background, b. low b value of 50 sec/mm² hypointense with hyperintense foci of necrosis , c. b value 400 sec/mm² overall increased intensity , d. high b value 800 sec/mm² more increased intensity , e. hypointense in ADC map showing low ADC value, f. , g. early contrast, showed heterogeneous mosic enhancement , h. late contrast showing capsule enhancement.

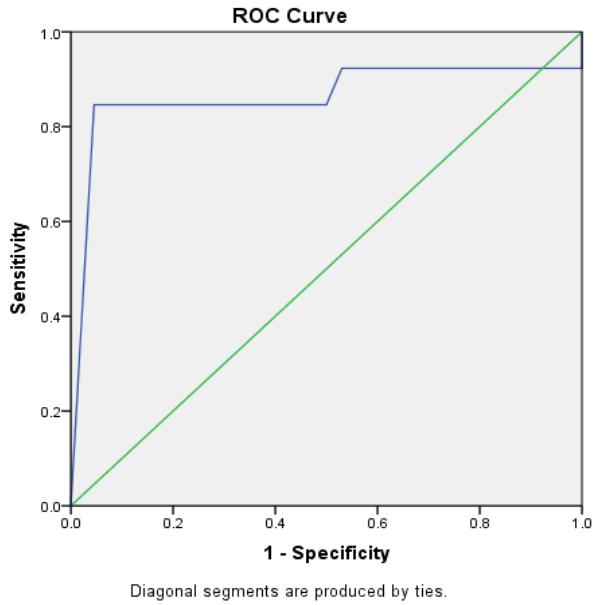


**Figure 7.** The receiver operating characteristic (ROC) curve showed a highly significant association between the diagnosis of liver diseases and ADC value (P-value of <0.001). Area under the curve was (0.864) and the standard error of mean (SEM) was (0.042). We used a cutoff point of 1.5 for ADC value.

## References

1. Demir Ö, Obuz F, Sağol Ö et al. Diagn Interv Radiol 2007; 13:81-86.
2. Lincke T, Zech C. Liver metastases: Detection and staging. European Journal of Radiology. 2017;97:76-82.
3. Goshima S, Kanematsu M, Kondo H, Yokoyama R, Kajita K, Tsuge Y et al. Diffusion-weighted imaging of the liver: Optimizing b value for the detection and characterization of benign and malignant hepatic lesions. Journal of Magnetic Resonance Imaging. 2008;28:691-697.
4. Robinson P, Ward J. MRI of the liver. New York: Taylor & Francis; 2006.
5. Silva A, Evans J, McCullough A, Jatoi M, Vargas H, Hara A. MR Imaging of Hypervascular Liver Masses: A Review of

Current Techniques. RadioGraphics. 2009;29:385-402.
6. Thoeny H, De Keyzer F. Extracranial applications of diffusion-weighted magnetic resonance imaging. European Radiology. 2007;17:1385-1393.
7. Le Bihan D, Turner R, Douek P, Patronas N. Diffusion MR imaging: clinical applications. American Journal of Roentgenology. 1992;159:591-599.
8. Hagmann P, Jonasson L, Maeder P, Thiran J, Wedeen V, Meuli R. Understanding Diffusion MR Imaging Techniques: From Scalar Diffusion-weighted Imaging to Diffusion Tensor Imaging and Beyond. RadioGraphics. 2006;26:S205-S223.
9. Müller M, Prasad P, Siewert B, Nissenbaum M, Raptopoulos V, Edelman R. Abdominal diffusion mapping with use of a whole-body echo-planar system. Radiology. 1994;190:475-478.
10. Taouli B, Sandberg A, Stemmer A, Parikh T, Wong S, Xu J et al. Diffusion-weighted imaging of the liver: Comparison of navigator triggered and breathhold acquisitions. Journal of Magnetic Resonance Imaging. 2009;30:561-568.
11. Kele P. Diffusion weighted imaging in the liver. World Journal of Gastroenterology. 2010;16:1567.
12. Tokgoz O, Unlu E, Unal I, Serifoglu I, Oz I, Aktas E et al. Diagnostic value of diffusion weighted MRI and ADC in differential diagnosis of cavernous hemangioma of the liver. African Health Sciences. 2016;16:227.
13. Gelebek Yilmaz F, Yildirim A. Relative Contribution of Apparent Diffusion Coefficient (ADC) Values and ADC Ratios of Focal Hepatic Lesions in the Characterization of Benign and Malignant Lesions. European Journal of Therapeutics. 2018;24:150-157.
14. Kim T, Murakami T, Takahashi S, Hori M, Tsuda K, Nakamura H. Diffusion-weighted single-shot echoplanar MR imaging for liver disease. American Journal of Roentgenology. 1999;173:393-398.
15. Taouli B, Vilgrain V, Dumont E, Daire J, Fan B, Menu Y. Evaluation of Liver Diffusion Isotropy and Characterization of Focal Hepatic Lesions with Two Single-Shot Echo-planar MR Imaging Sequences: Prospective Study in 66 Patients. Radiology. 2003;226:71-78.
16. Fowler K, Brown J, Narra V. Magnetic resonance imaging of focal liver lesions: Approach to imaging diagnosis. Hepatology. 2011;54:2227-2237.
17. Ichikawa T, Haradome H, Hachiya J, Nitatori T, Araki T. Diffusion-weighted MR imaging with single-shot echo-planar imaging in the upper abdomen: preliminary clinical experience in 61 patients. Abdominal Imaging. 1999;24:456-461.
18. Chan J, Tsui E, Luk S, Fung A, Yuen M, Szeto M et al. Diffusion-weighted MR imaging of the liver: distinguishing hepatic abscess from cystic or necrotic tumor. Abdominal Imaging. 2001;26:161-165.
19. Parikh T, Drew S, Lee V, Wong S, Hecht E, Babb J et al. Focal Liver Lesion Detection and Characterization with Diffusion-weighted MR Imaging: Comparison with Standard Breath-hold T2-weighted Imaging. Radiology. 2008;246:812-822.
20. Soyer P, Corno L, Boudiaf M, Aout M, Sirol M, Placé V et al. Differentiation between cavernous hemangiomas and untreated malignant neoplasms of the liver with free-breathing diffusion-weighted MR imaging: Comparison with T2-weighted fast spin-echo MR imaging. European Journal of Radiology. 2011;80:316-324.
21. Namimoto T, Yamashita Y, Sumi S, Tang Y, Takahashi M. Focal liver masses: characterization with diffusion-weighted echo-planar MR imaging. Radiology. 1997;204:739-744.
22. Yang D, Zhang J, Han D, Jin E, Yang Z. The role of apparent diffusion coefficient values in characterization of solid focal liver lesions: a prospective and comparative clinical study. Science China Life Sciences. 2017;60:16-22.
23. Moteki T, Horikoshi H, Oya N, Aoki J, Endo K. Evaluation of hepatic lesions and hepatic parenchyma using diffusion-weighted reordered turboFLASH magnetic resonance images. Journal of Magnetic Resonance Imaging. 2002;15:564-572.
24. Onur M, Çiçekçi M, Kayalı A, Poyraz A, Kocakoç E. The role of ADC measurement in differential diagnosis of focal hepatic lesions. European Journal of Radiology. 2012;81:e171-e176.