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ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA

Diffusion-weighted MRI: In differential diagnosis of liver masses

Karaciğer kitlelerinin ayırıcı tanısında difüzyon ağırlıklı MRG

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ABSTRACT

Objectives: The purpose of our study was to determine apparent diffusion coefficients (ADCs) of focal liver lesions on the basis of respiratory triggered diffusion-weighted single-shot echo-planar MR imaging (DWI-SS-EPI) sequence and to evaluate whether ADC measurements can be used to characterize lesions.

Patients and Methods: One hundred and eighteen patients with 134 focal liver lesions [35 cysts, 48 hemangiomas, 4 focal noduler hyperplasias (FNH), 31 metastases, 14 hepatocellular carsinomas (HCCs), 1 fibrolamellar carsinoma, 1 cholangiocellular carcinoma; mean size 18.4 mm; range 10-140 mm] were examined on a 1.5-T system using respiratory triggered DWI-SS-EPI (b-values: 50, 400, 800 s/mm^2).

Results: Results were correlated with characteristic MRI findings, histopathologic data and follow-up imagings. The ADCs of different lesion types were compared and lesion differentiation using optimal thresholds for ADCs was evaluated. Mean ADCs (x10^{-3} mm^2/s) were 2.15, 1.57, 1.16, 1.08, 1.03 for cysts, hemangiomas, FNHs, metastases and HCCs, respectively. Mean ADCs differed significantly for all lesion types except metastases, HCCs and FNHs. Overall, 88.5% of lesions were correctly classified as benign or malignant using a treshold value of 1.20x10^{-3}mm^2/s.

Conclusion: Measurements of the ADCs of focal liver lesions on the basis of a respiratory triggered DWI-SS-EPI sequence may constitute a useful supplementary method for lesion characterization.

Keywords: Respiratory triggered diffusion-weighted single-shot echo-planar magnetic resonance imaging technique, Apparent diffusion coefficients, Focal liver lesions

ÖZ

Amaç: Çalışmamızın amacı, solunum tetiklemeli single-shot echo-planar difüzyon (DW-SS-EPI) magnetik rezonans görüntüleme (MRG) tekniği ile, karaciğer lezyonlarının 'görünür difüzyon katsayısı (ADC)'nı ölçmek ve lezyonların ayırıcı tanısına katkısını araştırmaktır.

Hastalar ve Yöntem: Çalışmada 118 hasta ve 134 fokal karaciğer kitlesi [35 kist, 48 hemanjiom, 4 fokal noduler hiperplazi (FNH), 31 metastaz, 14 hepatoselüler karsinom (HCC), 1 fibrolamellar karsinom, 1 kolanjioselüler karsinom; ortalama boyut, 18.4 mm; range 10-140 mm] 1.5 T, solunum tetiklemeli DW-SS-EPI MR tekniği ile incelendi (b değerleri: 50, 400, 800 s/mm^2). Tanılar karakteristik MR bulguları, histopatolojik veri ve takip görüntülemelerle konuldu. Farklı karakterdeki tüm lezyonların ADC değerleri ayrı ayrı ölçüldü ve lezyonların ayırıcı tanısı için eşik ADC değerleri belirlendi.

Bulgular: Ortalama ADC değerleri (x10^{-3} mm^2/s); 2.15, 1.57, 1.16, 1.08, 1.03 olup, sırasıyla kist, hemanjiyom, FNH, metastaz, HCC' ye aittir. Ortalama ADC değerleri, metastazların FNH ve HCC'lerden ayırımı dışındaki tüm lezyonların ayırıcı tanısında anlamlıdır. Eşik ADC değeri 1.20x10^{-3} mm^2/s olarak alındığında, tüm lezyonların % 88,5'inin benign-malign ayırımı yapılabilmiştir.

Sonuç: Fokal karaciğer kitlelerinin ayırıcı tanısında, solunum tetiklemeli DW-SS-EPI sekansıyla ölçülen ADC değerleri, ayırıcı tanıda oldukça etkin bir yöntemdir.

Anahtar Kelimeler: Solunum tetiklemeli single-shot echo-planar difüzyon MR görüntleme tekniği, Görünür difüzyon katsayısı, Fokal karaciğer kitleleri

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Introduction

Magnetic resonans imaging (MRI) is the most common modality in differantial diagnosis of liver lesions. Contrast enhanced dynamic MRI has an indispensable role for characterization of liver masses. In recent years, additional MRI sequences have been used as diffusion-weighted magnetic resonans imaging (DWI MRI). It is a fast, no contrast administered technique that enables functional data about liver masses in addition to morphologic data [1-3]. Spin echo echo-planar imaging (SE-EPI) sequence with single shot breath holding tecnique is performed in DWI. With the development of paralel imaging techniques, imaging time has become shorter, quality of EPI sequence has increased and addition of DWI to routine abdominal imaging has become more effective and popular [4-6]. Recent studies have shown the efficacy of quantitative apparent coefficient diffusion (ADC) measurements in differential diagnosis of benign and malignant liver masses [7-9]. According to literature, differential diagnosis of benign and malignant liver masses with the aid of DWI, is possible with acceptable accuracy [7-9].

In this prospective study, we aimed to evaluate whether ADC measurements can be used to characterize liver masses.

Patients and Methods

Study population

DWI MRI was performed in the patients who had pimary or secondary, malignant or benign liver lesions between January 2008 and February 2009 in a university hospital. Patients who have contraindications for MRI imaging were excluded in the study. Inclusion criteria were as follows; Liver lesions incidentally detected during routine abdominal ultrasonography (US) or routine abdominal computed tomography (CT) scans. Eighteen patients who had incidental masses on US were recalled to perform liver MRI with DWI sequence.

An approval by Institutional Review Board of the School of Medicine was obtained. Each patient signed a written informed consent.

MRI imaging

All DWI MRI images were obtained using a 1.5 Tesla MR (Magnetom Vision: Siemens Healthcare, Erlangen, Germany) with a phased-array coil. Conventional sequences of routine upper abdominal MRI were performed for all patients. The sequences used for the conventional MRI were; axial fat-suppressed T2-weighted (TR/TE, 2700/93 ms; flip angle, 170°; slice thickness, 8 mm; FOV, 400 mm), T2- weighted turbo spin echo (TSE) (TR/TE, 3100/179 ms), T1 weighted in-phase and out-of-phase gradient echo (TR/TE, 192/5 ms for in-phase, 250/70 ms for out-of-phase); flip angle 80°, slice thickness, 8 mm) and contrast-enhanced dynamic axial T1-weighted three-dimentional volumetric interpolated breath-hold examination (VIBE) sequences (TR/TE, 5.32/2.45 ms; flip angle, 10°, slice thickness 1 mm). Gadoterate meglumine (Dotarem®, Laboratoire Guerbet, Roissy, France) or gadobutrol (Gadovist®, Bayer Healthcare, Berlin, Germany) were used as contrast media. Contrast media was administered intravenously over 20 s by an automatic MR-compatible injector with a 0.1 mmol/kg dose.

The DWIs were performed before the contrast enhanced sequences with a two-dimentional, axial, echo planar imaging (EPI) sequences (TR/TE, 4600/81, flip angle 90°, slice thicness, 5 mm, FOV, 400 mm, fat saturated). The sensitizing diffusion gradients were in three ortogonal planes with three different b values (b=50, b=400, b=800 s/mm^2). The ADC map images were created automatically by the system. The ADC values were calculated according to the following formula: ADC=1/(b2-b1)×ln(S1/S2) where the S1 and S2 values were the signal intensities at the b values of b1=50 and b2=800 s/mm^2, respectively.

Lesion assessment

Lesions which are equal to or larger than 10 mm were included in this study. A single measurement was made for lesions with a diamater equal to 1.0 cm and three different measurements were performed for lesions over 1.0 cm. In lesions bigger than 1.0 cm, mean diameter was taken into consideration. All lesions were evaluated by two radiologists (R. E and D. T) with four and fifteen years of experience in abdominal radiology , respectively. The readers were blinded to the final histopathological results. Contrast-enhanced images were used as reference images in evaluating the masses because they had better resolution. The shapes, margins, signal intensity, and contrast enhancement patterns of lesions were evaluated. The DWI images were analyzed to observe any restriction of diffusion in the lesions, and the ADC maps were used for ADC measurements. The enhanced part of the lesions on contrast enhanced images was preferred for evaluation on the corresponding DWI-MRI; the region of interest (ROI) was placed manually on the corresponding area of the ADC map. A standard 1 cm^2 diameter circular ROI was used. The diagnostic performance was evaluated by calculating the area under the receiver operating characteristics curve (AUC) and optimal cut-off values.

Statistical analysis

The statistical analysis was performed using a commercially available software (Statistical Package for Social Sciences, version 15.0, SPSS Inc., Chicago, Illinois, USA). The mean ADC values of independent groups were compared using Student's t test. For continous variable; ADC values were given as mean±standard deviation. The ROC analysis was performed to find threshold ADC values to differentiate liver lesions. $P < 0.05$ was considered statistically significant.

Results

Of the total 134 mass, 87 (64%) were benign and the mean diameter of these benign lesions was 22,2±16.53 mm. The mean ADC for all benign lesions were 1.78±0.68x10^{-3} mm^2/s, between a range of 1.16±0.06x10^{-3} and 2.15 ±0.88x10^{-3} mm^2/s.

The cystic lesions had the highest ADC value. Among all benign masses, focal nodular hyperplasia (FNH) had the lowest ADC value (Figure 1 a-d). ADC values of all types of benign masses were given individually on Table I.

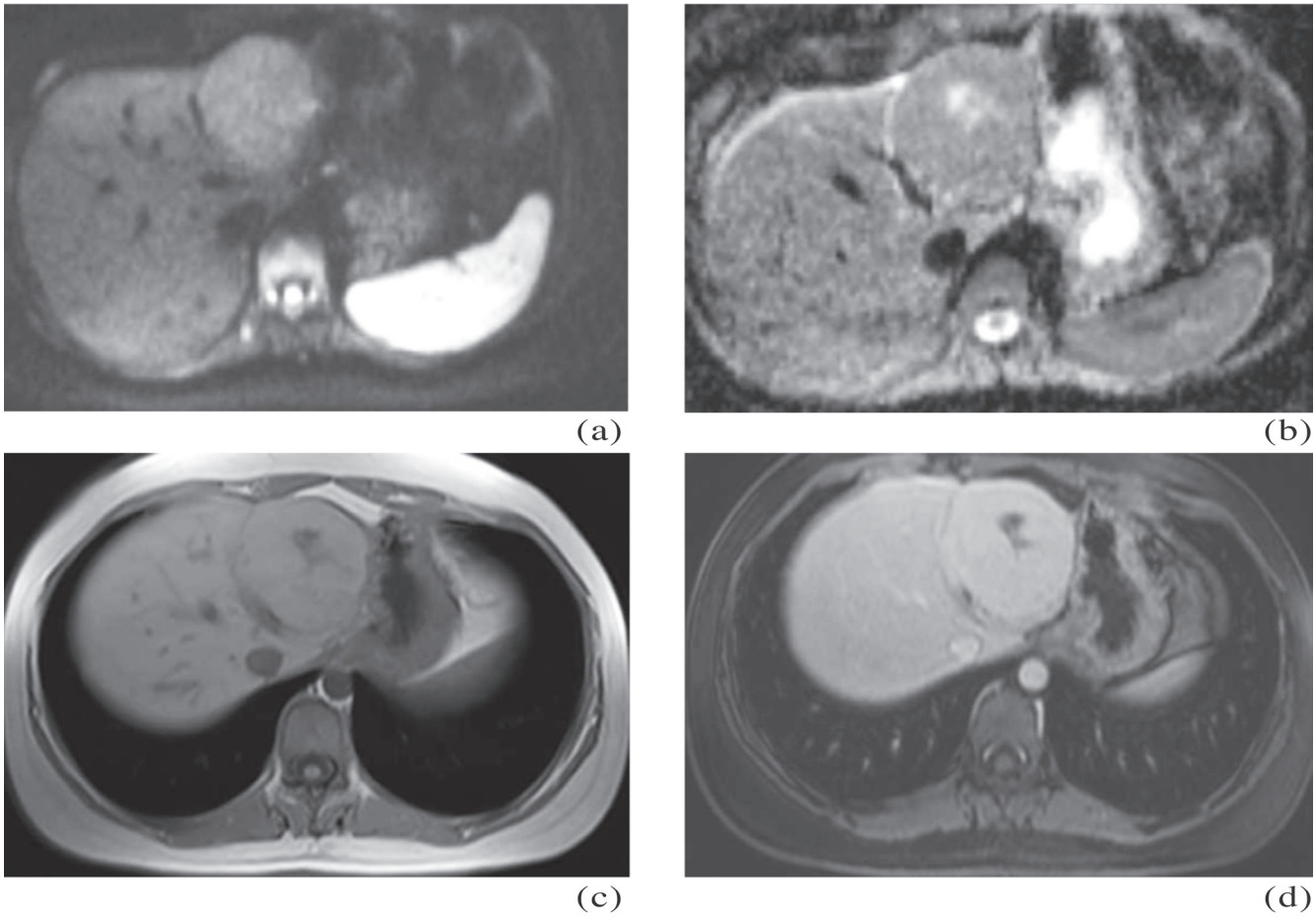

Figure 1. a-d. A forty-nine year old female with the histopathological diagnosis of focal nodular hyperplasia (FNH). On DWI with b value of 800s/mm^2 **(a)** and ADC map **(b)** diffusion restriction of the mass is seen. ADC value for the lesion was 1.11x10^{-3} mm^2/s. On conventional axial T1-weighted non-contrast-enhanced **(c)** and contrast-enhanced **(d)** images, we can see the typical morphological features of FNH.

Table I: ADC values of benign masses

Lesion size	Number of lesions	Mean ADC value (x$10^{-3}$$mm^2/s$)
Basic cyst	35	2.15±0.88
Hemangioma	48	1.57±0.34
FNH	4	1.16±0.06

FNH: Focal Nodular Hyperplasia

The difference between the mean ADC values of hemangiomas and cystic lesions was statistically significant in our study ($p<0.001$). However, the ADC values of these two lesions were matching at some points (Figure 2). If the cut-off ADC value was 1.74x10^{-3} mm^2/s to differentiate hemangiomas and cystic lesions, the sensitivity and specificity were 68% and 71% respectively.

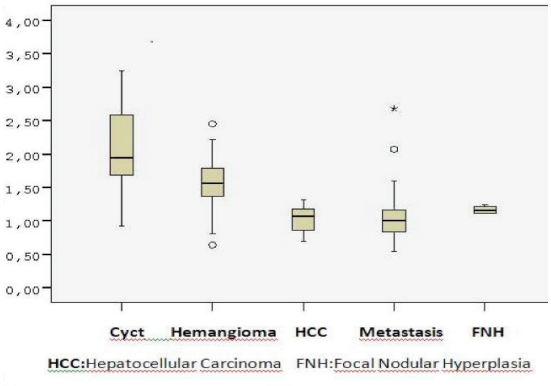

Figure 2: ADC values of benign and malignant lesions

Of the total 134 masses, 47 (64%) were malignant and the mean diameter of these malignant lesions was 42.0±11.1 mm. The mean ADC values for all malignant lesions were 1.08±0.36 mm^2/s mm^2/s, between a range of 1.03±0.2 and 1.51±0.42 mm^2/s. Cholangiocarcinomas had the highest ADC values, hepatocellular carcinoma (HCC) had the lowest ADC value among all malignant lesions (Table II). Although cystic metastatic masses were malignant, there was no statistically significant difference between the ADC values of these metastatic cysts and simple liver cysts ($p<0.66$) (Figure 3).

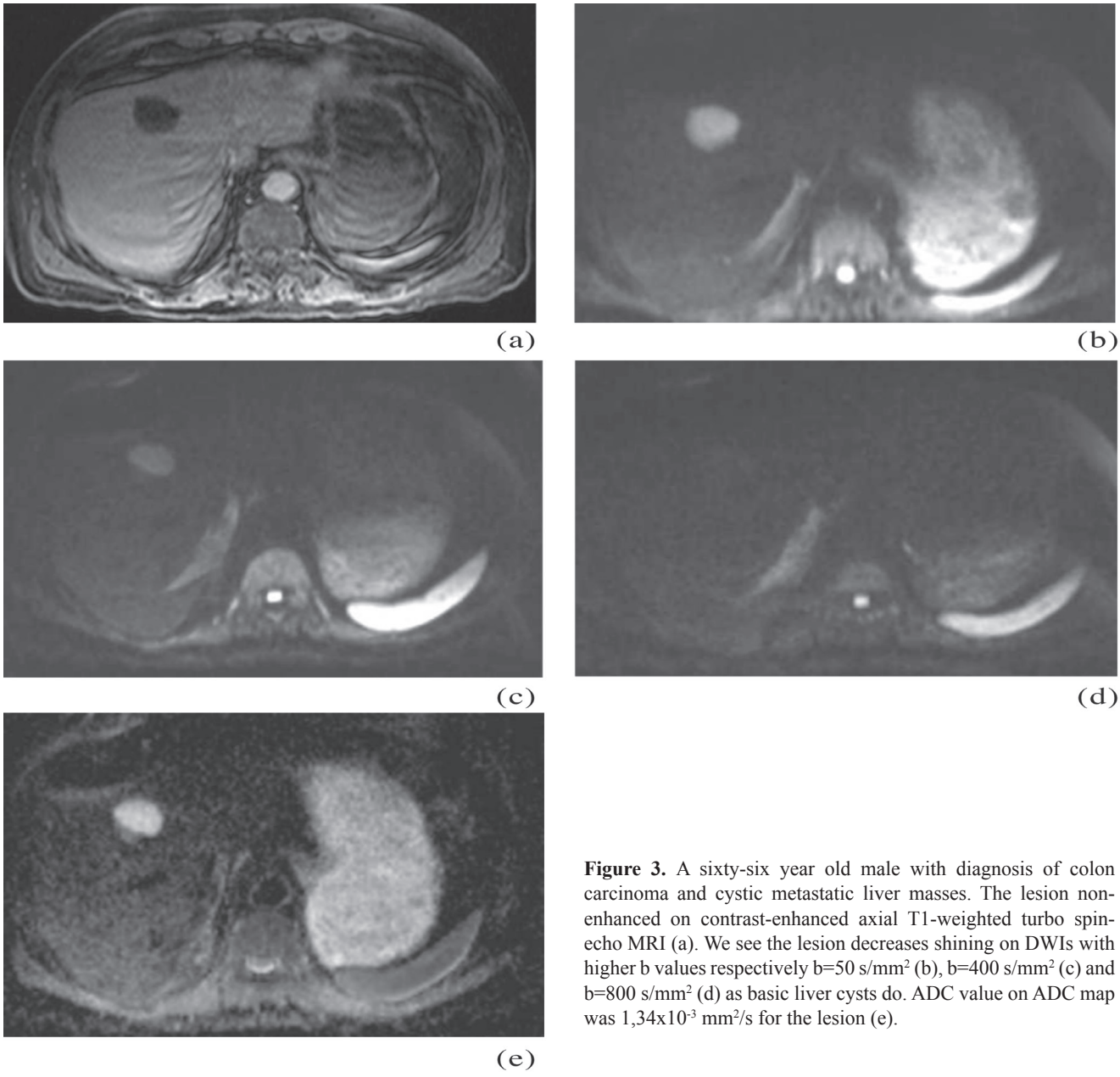

Figure 3. A sixty-six year old male with diagnosis of colon carcinoma and cystic metastatic liver masses. The lesion non-enhanced on contrast-enhanced axial T1-weighted turbo spin-echo MRI (a). We see the lesion decreases shining on DWIs with higher b values respectively b=50 s/mm^2 (b), b=400 s/mm^2 (c) and b=800 s/mm^2 (d) as basic liver cysts do. ADC value on ADC map was $1,34x10^{-3}$ mm^2/s for the lesion (e).

Table II: ADC values of malignant lesions

Type of lesions	Number of lesions	Mean ADC Value (x10-^{3}mm^2/s)
Metastases	31	1.08±0.42
Hepatocellular carcinoma	14	1.03±0.2
Fibrolamellar carcinoma	1	1.15
Cholangiocarcinoma	1	1.51

The difference between hemangiomas and metastatic masses was statistically significant (Table IV). According to ROC analysis, using a threshold ADC value as 1.33x10^{-3} mm^2/s, lesions were differentiated with a 81% sensitivity and 86% specificity. The difference between the mean ADC values of hemangiomas and hepatocellular carcinomas was statistically significant. Hemangiomas and hepatocellular carcinomas were diagnosed differently, using a threshold ADC value of 1.26x10^{-3} mm^2/s, with a sensitivity of 85% and specificity of 86% (Table III).

Table III: Differentiation of hemangioma from HCC and metastasis

Differential diagnosis	Cut-off ADC Value (x10^{-3}mm^2/s)	Sensitivity (%)	Specificity (%)	P value
Hemangioma – Metastasis	1.33	81	81	<0.001
Hemangioma – HCC	1.26	85	86	<0.001

HCC: Hepatocellular carcinoma

There was no statistically significant difference between the ADC values of HCCs and metastatic masses (p<0.66). The mean ADC value of FNHs was higher than metastatic masses and HCCs, but there was no statistically significant difference between the FNHs and metastatic masses or HCCs (p<0.76).

There was statistically significant difference between the ADC values of benign and malignant lesions. According to ROC analysis, using a threshold ADC value of 1,20x10^{-3} mm^2/s, benign and malignant lesions were diagnosed differently with a %88.5 sensitivity and %81 specificity (Table IV, Figure 4)

Table IV: Differentation of lesions

Differential diagnosis	Cut-off ADC Value (x10^{-3}mm^2/s)	Sensitivity (%)	Specificity (%)	P Value
Benign - Malignant	1.2	88.5	81	<0.001
Hypervascular - Hypovascular	1.15	70	70	<0.001

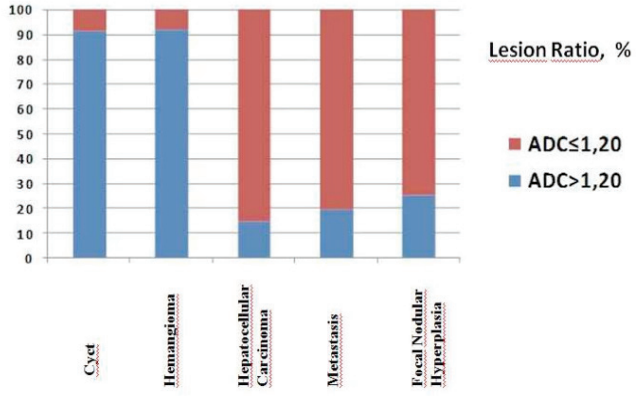

Figure 4: ADC values of all lesions

Eight of benign masses, had ADC values lower than 1.20x10^{-3} mm^2/s. Three of them were diagnosed as FNH and five were as hemangioma. Eight of all malignant lesions had ADC values higher than 1.20x10^{-3} mm^2/s. Four of these 8 masses were atypical malignant lesions and were diagnosed as cystic metastasis (n=2 colon carcinoma, n=1 gastric carcinoama, n=1 lung carcinoma), one of them was diagnosed as cholongiocarcinoma and two of them were as HCC. The ADC values of other metastatic lesions were lower than the threshold ADC values. Additionally, we differentiate the lesions as hypervascular (hemangioma, FNH, hypervascular metastasis, HCC, fibrolamellar carcinoma) and hypovascular masses (hypovascular metastasis, cholangiocarcinoma). There was statistically significant difference between mean ADC values of hyper-hypovascular masses (p<0.001 (Table IV). Hypervascular and hypovascular masses were diagnosed differently using a threshold ADC value of 1.15x10^{-3} mm^2/s, with a 70% sensitivity and 70% specificity (Figure 5).

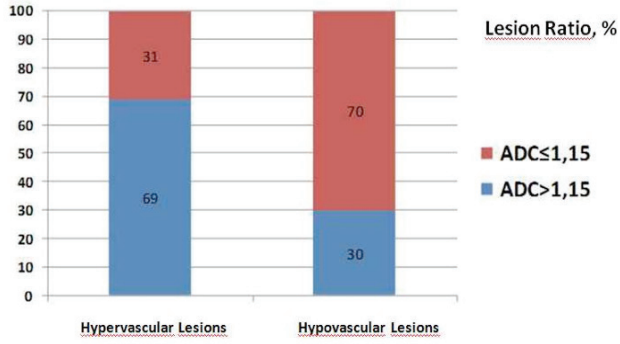

Figure 5: ADC values of hyper-hypovascular lesions

Discussion

The current study revealed that the DWI MRI has diagnostic accuracy to differentiate benign and malignant liver masses as Demir *et al*, Ichikawa *et al*, Bruegel *et al* revealed [7-9]. However, the threshold value to differentiate the benign and malignant lesions in our study was lower than literature due to the differences between the patient population and standard ‘’b’’ values and using different techniques for creating ADC maps. As we used the b values of 50 and 1000 to create the ADC maps, the perfusion effect is minimal. We think this may be another reason of finding lower ADC values than literature. The threshold ADC values to differentiate benign and malignant lesions was $1.63x10^{-3}$ mm^2/s in the literature and we found the threshold ADC value of $1.20x10^{-3}$ mm^2/s in our study. The sensitivity and specificity values of our study were approximately the same as the values in the literature. Hence, we think the threshold ADC value of $1.20x10^{-3}$ mm^2/s can be used to differentiate the benign and malignant lesions of the liver.

In addition to the literature, we classified all lesions into two groups as hypervascular (hemangioma, FNH, hypervascular metastasis, HCC, fibrolamellar hepatocellular carcinoma) and hypovascular (hypovascular metastasis, cholangiocarcinoma) solid lesions. We found that, these lesions could be differentiated with 70% sensitivity and specificity with the threshold ADC value of $1.15x10^{-3}$ mm^2/s.

In all lesions, the highest ADC values were in cysts and hemangiomas. The lowest ADC values were in HCCs. There was no adenoma or liver abscess in our study as benign liver lesions. There were three hydatid cysts which were classified as type 2 and 3 cysts. Contrary to Inan *et al*’s study, there were no statistically significant differences between the ADC values of basic liver cysts and hydatid cysts in our study [10]. Hence, we considered hydatid cysts as basic liver cysts for statistical analysis in our study. But the number of the cystic lesions was not high enough to make statistical analysis.

In daily practice, it is difficult to differentiate hemangiomas and metastasis from each other. As defined in the literature, we found that these lesions can be differentiated from each other by using DWI sequence and ADC maps. However, there were matching ADC values in differentiation of these lesions. This may be due to the similar hypervascular characteristics of hypervascular metastasis and hemangiomas. The difference between the ADC values of hypovascular metastasis and hemangiomas was statistically significant in our study. On the other hand, the difference between the ADC values of hypervascular metastasis and hemangiomas was not statistically significant in our study. This may be due to the greater ADC values of hypervascular metastasis. As we know, this was firstly defined in the literature [8-9].

Altough FNHs are benign lesions, they had low ADC values similiar with malignant lesions because of their hypercellular characteristics. In our study, there was no significant difference between FNHs and metastasis and between FNHs and HCCs statistically . However, the number of the FNHs was not enough to make a statistical analysis. As another limitation, there was no hepatic adenoma in our study. Hence, we had no contrubition to the literature about differentiating FNHs and adenomas.

In conclusion, DWI is a practical sequence which does not require contrast administration and has a considerable value in differentiation of benign and malignant lesions.

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