The accuracy of Diffusion Weighted Magnetic Resonance Imaging in differentiation of malignant from benign gynecologic lesions

Pelvik kitlelerin malign – benign ayırımında Difüzyon Ağırlıklı MRG bulguları

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ÖZET

GİRİŞ ve AMAÇ: Bu çalışmanın amacı jinekolojik lezyonlarda benign malign ayrımında Difüzyon Ağırlıklı MR incelemenin doğruluğunu araştırmaktır.
YÖNTEM ve GEREÇLER: Çalışmaya pelvik kitle ön tanısıyla alt batın MRG tetkiki istenen toplam 125 olgu dâhil edildi.MR görüntülemeri 1,5 Tesla görüntüleme sisteminde yapıldı. Bu hastalardan DAG ile sırasıyla b100, b600, b1000 gradient değerlerinde difüzyon ağırlıklı EPI görüntüler alındı. Pelvik kitle saptanan olgularda lezyonlardan ADC değerleri ölçüldü,125 jinekolojik lşezyonda ortalama kitle ADC değerleri karşılaştırıldı.
BULGULAR: Malign lezyon saptanan 35 olgunun lezyona ait ADC değerleri (b100, b600, b1000) (2.18x10–3; 1.47x10–3; 1.22x10–3), benign lezyon saptanan 90 olgunun lezyona ait ADC değerlerinden (b100, b600, b1000) (2.60x10–3; 2.05x10–3; 1.79x10–3 mm2/sn) düşük olup aradaki fark istatistiksel olarak anlamlı bulunmuştur (p<0,05). Ayrıca benign-malign ayrımını yapmamızı sağlayabilecek bir kestirim noktası araştırıldı ve 1.6x10–3 mm2/s nin b100 değeri için %40 duyarlılık ve %88 özgüllük ile; 1.4x10–3 mm2/s ADC değerinin b600 gradientinde % 57duyarlılık %77 özgüllük ile; ve 0.9x10–3 mm2/s değerinin b1000 gradientinde %57 duyarlılık ve %91 özgüllük gösterdiği görüldü. Bu analizler sonucu b1000 ADC değerinin jinekolojik lezyonların benign-malign ayrımında en yüksek doğruluğa sahip olduğu görüldü.
TARTIŞMA ve SONUÇ: ADC değer ölçümleriyle birlikte difüzyon MRG bir fonksiyonel görüntüleme yöntemi olarak kitlelerin malign-benign ayırımında önemli katkılar sağlayabilmektedir.
Anahtar Kelimeler: Manyetik Rezonans Görüntüleme, Pelvik kitle, Difüzyon Ağırlıklı Görüntüleme, ADC, Jinekolojik lezyon

ABSTRACT

INTRODUCTION: The aim of the present study was to investigate the accuracy of diffusion weighted magnetic resonance imaging (DWI) in differentiation of malignant from benign gynecologic lesions.
METHODS: A total of 125 patients who underwent pelvic MRI with an initial diagnosis of gynecologic mass included in the study. The MRI examinations were performed on a 1.5 Tesla MR imaging system. The DWI protocol included water excitation with three b values (100, 600 and 1000s/mm2) and apparent diffusion coefficient (ADC) maps were created. Mean ADC values were calculated in 125 gynecologic lesions.
RESULTS: We observed significantly lower ADC values in malignant lesions compared with benign ones in all b values (p= 0.047 for b100, p<0.001 for b600, p<0.001 for b1000). We also evaluated the cut-off points of ADC value for differentiation of malignant from benign lesions and observed 1.6x10–3 mm2/s for b100 with a sensitivity of 40% and a specificity of 88%; 1.4x10–3 mm^2/s for b600 with a sensitivity of 57% and a specificity of 77%, and 0.9x10–3 mm^2/s for b1000 with a sensitivity of 57% and a specificity of 91%. According to these analyses, ADC value at b1000 was found to have the highest accuracy for differentiation of malignant from benign gynecologic lesions.
DISCUSSION and CONCLUSION: ADC measurements can be used for differentiation of malignant from benign gynecologic lesions.
Keywords: Magnetic Resonance Imaging (MRI), Pelvic mass, Diffusion Weighted Imaging (DWI), ADC, Gynecologic lesion

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INTRODUCTION

Endometrial, cervical and ovarian carcinomas are the most common three gynecologic malignancies of the world. These malignancies are the leading causes of mortality and morbidity in women after breast cancer. Even so, endometrial carcinoma has the highest curability within the most common 10 female malignancies (1). The detection of these malignancies depends on clinical findings and diagnostic imaging methods. The first imaging method for a suspected gynecologic malignancy is ultrasonography which is used to confirm a mass, identify the originating organ and characterize the mass. Despite the useful information accuired with US, magnetic resonance imaging (MRI) is superior because of its soft tissue contrast especially in uterin and cervical lesions (2) and used as a problem solving modality in patients with sonographically undetermined lesions (3).

Conventional MRI has been widely accepted as a valid imaging modality for gynecologic masses. Although the morphologic features of a lesion like solid component or papillary projections for ovarian carcinoma and signal intensity changes for endometrial or cervical carcinoma would be helpful in differentiating a lesion, microstructural changes which would be helpful for characterizing a lesion can not be evaluated with conventional MRI. Diffusion weighted imaging (DWI) is a noninvasive MRI technique which is promising for showing microstructural changes, early tumor detection and evaluation of treatment responce (4). There are numerous studies investigating the accuracy of DWI in differentiating benign lesions from ovarian cancer (5-7), endometrial cancer (8, 9), and cervical cancer (10-12). However there is not one study available in the literature which investigates the accuracy of DWI in differentiating malignant from benign lesions which include most of gynecologic lesions. The aim of the present study was to investigate the accuracy of DWI in differentiation of malignant from benign gynecologic masses.

PATIENTS and METHODS

A total of 125 female patients who referred to our department for pelvic MRI with a suspected gynecologic mass between October 2007 and October 2008 were included in this study. All patients gave written informed consent for MRI examination. This study was approved by our instutitional review board.

From the study patients, 67 were operated and 58 were followed up. According to the histopathologic evaluation and follow up results, the final diagnosis was malignant for 35 lesions and 90 lesions benign. The malignant lesions were endometrial carcinoma in 5 patients (4%) cervical carcinoma in 12 patients (9.6%) and ovarian carcinoma in 18 patients (14.4%). The benign lesions were leiomyom in 28 patients (22.4%), endometrioma in 12 patients (9.6%), hemorrhagic ovarian cyst in 12 patients (9.6%), follicular cyst in 11 patients (8.8%), lymphocel in 9 patients (7.2%), dermoid tumour in 8 patients (6.4%), benign ovarian tumour in 5 patients (4%), and nabothi cyst in 5 patients (4%) (Table 1).

MR examination

All patients underwent pelvic MRI with a 1.5 Tesla MR unit (Signa Hispeed Excite General Electric, Milwaukee, WI). The patients were examined in supine position. Diffusion-weighted MR images were obtained by a 4-channel phased array coil for body, using an echo planar imaging in the axial plane without breath holding in approximately 30 seconds. A three-plane gradient echo localizer sequence was performed at the beginning of the examination. Imaging parameters were repetition time (TR)/ echo time (TE): 8000/80 ms; section thickness: 5 mm; intersection gap: 0; matrix size: 128 x 128; field of view: 300 x 300 mm, water excitations with b values of 100, 600 and 1000 s/mm^2 for DWI. Axial T2 weighted spin-echo sequences (TR/TE= 4100/95, section thickness: 5 mm; intersection gap: 1 mm) were also performed for lesion detection. T2 weighted images were used for detection of lesion and lesion diameters. Color-coded ADC maps were automatically created by the diffusion difference between gradients *b* 100, *b* 600 and *b* 1000 s/mm^2 and the *b* 0 gradient on a workstation (Advantage Windows, software version 2.0, General Electric Medical Systems). Monoexponential method was used in ADC measurements. A minimum mean square error estimator was

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used in the monoexponential method to minimize the mean square error of the fitted ADC values. The mean ADC values were calculated on images with all acquired *b* values. A round or elliptical region of interest (ROI) with an area range between 50-70 mm^2 was placed by a radiologist (M.B. with 4 years of experience) on color-coded ADC maps of the detected lesions. The ROIs were placed in the centre of pure cystic lesions, the solid component of complex cystic lesions and the markedly diffusion restricted area of degenerate leiomiomas and solid masses (Figure 1).

Lesions were divided into two major groups according to histopathological analyses and follow-up results as malignant lesions and benign lesions. Calculated ADC values for *b* values of 100, 600 and 1000 s/mm^2 were compared for major groups and subgroups.

Statistical analyses

Data was summarized as mean ± standard deviation for continuous variables and frequencies for categorical variables. Mann Whitney U test was used for independent group comparisons depending on the distributional properties of the data. A p value <0.05 was considered as statistically significant. In order to determine the diagnostic accuracy of ADC measurements, ROC analysis was performed. Cut-off ranges were calculated around the optimal cut-off to maximize sensitivity and specificity for discrimination of malignant from benign gynecologic lesions. Youden index J values were used to compare diagnostic accuracy of ADC measeurements in different *b* values.

RESULTS

A total of 125 female patients with mean age of 39 (range: 16-75) were included in this study. The final diagnosis was made according to histopathologic evaluation (n= 67) or follow up results (n=58). Lesions were divided into two major groups; malignant lesions (n= 35) and benign lesions (n=90).

The mean and standard deviation (SD) of ADC values ($x10^{-3}$ mm^2/s) of all lesions were 2.48±0.9 for *b* 100, 1.89±0.7 for *b* 600, and 1.63±0.8 for *b* 1000. The mean and SD of ADC values ($x10^{-3}$ mm^2/s) of malignant lesions were 2.18±0.6 for *b*100, 1.48±0.4 for *b*600, and 1.22±0.2 for *b*1000. The mean and SD of ADC values ($x10^{-3}$ mm^2/s) of endometrial carcinoma were 1.85±0.5 for *b* 100, 1.16±0.7 for *b* 600, and 0.91±0.1 for *b* 1000. The mean and SD of ADC values ($x10^{-3}$ mm^2/s) of cervical carcinoma were 2.14±0.6 for *b* 100, 1.19±0.4 for *b* 600, and 0.87±0.1 for *b* 1000. The mean and SD of ADC values ($x10^{-3}$ mm^2/s) of ovarian carcinoma were 2.27±0.6 for *b* 100, 1.73±0.5 for *b* 600, and 1.51±0.1 for *b* 1000.

The mean and SD of ADC values ($x10^{-3}$ mm^2/s) of benign lesions were 2.60±0.8 for *b* 100, 2.05±0.5 for *b* 600, and 1.79±0.2 for *b* 1000. The highes ADC values were detected in lymphocels (3.87±0.9 for *b* 100, 3.05±0.9 for *b* 600, and 2.86±0.1 for *b* 1000) and lowest ADC values were detected in endometriomas (1.84±0.5 for *b* 100, 1.42±0.3 for *b* 600, and 1.15±0.2 for *b* 1000). The ADC values of all patients are summarized in Table 1.

The ADC values according to the variable *b* values were significantly different for malignant and benign masses (p<0.001) (Figure 2). There were significantly lower ADC values in malignant lesions in all *b* values (p= 0.047 for *b* 100, p<0.001 for *b* 600, p<0.001 for *b* 1000). The cut-off points of ADC value for differentiation of malignant from benign lesions were $1.6x10^{-3}$ mm^2/s for *b* 100 (area under the curve, 0.615, 95% confidence interval: 0.524, 0.701, Youden index J: 0.2889) with a sensitivity of 40% and a specificity of 88%; $1.4x10^{-3}$ mm^2/s for *b* 600 (area under the curve, 0.735, 95% confidence interval: 0.649, 0.810, Youden index J: 0.4016) with a sensitivity of 57% and a specificity of 77%, and $0.9x10^{-3}$ mm^2/s for *b* 1000 (area under the curve, 0.752, 95% confidence interval: 0.666, 0.824, Youden index J: 0.4825) with a sensitivity of 57% and a specificity of 91% (Table 4). According to these analyses, ADC value at *b* 1000 was found to have the highest accuracy for differentiation of malignant from benign gynecologic masses (Table 2, Figure 3).

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Table 1: The details of detected 125 gynecological lesions in 125 patients.

Final Diagnosis	Numbers	ADC values (10^{-3} mm^2/s) *b* 100 mean (±SD)	ADC values (10^{-3} mm^2/s) *b* 600 mean (±SD)	ADC values (10^{-3} mm^2/s) *b* 1000 mean (±SD)
Benign Gynecologic Lesions	**90**	**2.60 (±0.8)**	**2.05 (±0.5)**	**1.79 (±0.2)**
Benign ovarian tumour	5	2.84 (±0.6)	2.54(±0.6)	2.41(±0.3)
Endometrioma	12	1.84(±0.5)	1.42(±0.3)	1.15(±0.2)
Ovarian dermoid	8	2.35(±0.5)	1.72(±0.4)	1.52(±0.2)
Follicular cyst	11	3.39(±0.9)	2.72(±0.8)	2.45(±0.1)
Hemorrhagic cyst	12	2.70(±0.7)	2.32(±0.6)	2.10(±0.1)
Lymphocele	9	3.87(±0.9)	3.05(±0.9)	2.86(±0.1)
Leiomyoma	20	2.15(±0.6)	1.53(±0.5)	1.22(±0.1)
Degenerating Leiomyoma	8	1.94(±0.5)	1.59(±0.3)	1.10(±0.1)
Nabothian Cyst	5	2.74(±0.7)	2.03(±0.5)	1.93(±0.1)
Malignant Gynecologic Lesions	**35**	**2.18 (±0.6)**	**1.48 (±0.4)**	**1.22 (±0.2)**
Endometrial Carcinoma	5	1.85 (±0.5)	1.16 (±0.7)	0.91 (±0.1)
Cervical carcinoma	12	2.14 (±0.6)	1.19 (±0.4)	0.87(±0.1)
Ovarian carcinoma	18	2.27 (±0.6)	1.73 (±0.5)	1.51 (±0.1)

Table 2 Diagnostic accuracy of ADC measurement for estimation of malignant lesions

Patients Cut-off value	**AUC**	**Sensitivity (95% CI)**	**Specificity (95% CI)**	**PPV (95% CI)**	**NPV (95% CI)**	**p value**
***b*100** ≤1.6x10^{-3} s/mm^2	0.615 (0.524-0.701)	0.40 (0.24,0.58)	0.88 (0.80,0.94)	0.58 (0.37,0.78)	0.79 (0.70,0.87)	0.070
***b*600** ≤1.4x10^{-3} s/mm^2	0.735 (0.649-0.810)	0.57 (0.39,0.74)	0.77 (0.67,0.85)	0.49 (0.33,0.65)	0.82 (0.72,0.90)	<0.001
***b*1000** ≤0.9x10^{-3} s/mm^2	0.752 (0.666-0.824	0.57 (0.39,0.74)	0.91 (0.83,0.96)	0.71 (0.51,0.87)	0.85 (0.76,0.91)	<0.001

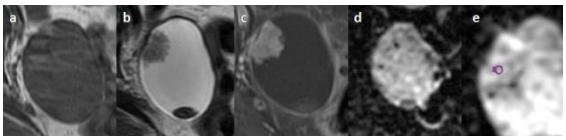

Figure 1: The MRI findings of serous papiller ovarian carcinoma in right ovary with irregular shaped solid component. The features of T1 weighted imaging (a), T2 weighted imaging (b), postcontrast fat saturation T1 weighted imaging (c), and diffusion restriction on DWI is seen. The measurement from solid component on ADC map reveals an ADC value of 0.67 x10^{-3} mm^2/s (e).

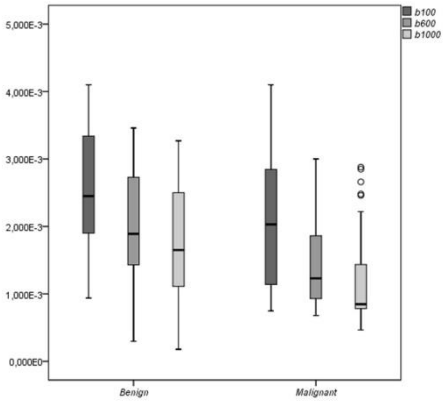

Figure 2: Box plot shows the different ADC values according to *b* 100, *b* 600 and *b* 1000 between malignant and benign gynecologic lesions.

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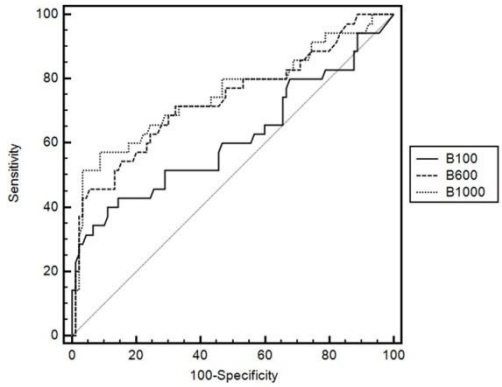

Figure 3: Graph shows ROC curve for discriminating malignant from benign gynecologic lesions.

DISCUSSION

Decreased ADC values have been reported in various malignities which can be explained by the increased cellular density of tissue (13-15). There are also various MRI studies which evaluate the accuracy of DWI in differentiation of specific gynecologic malignities like endometrial, cervical and ovarian carcinomas from benign lesions or other conditions. Tamai et al observed significantly lower mean ADC values in patients with endometrium carcinoma as compared with normal endometrium (0.88 ± 0.16 vs 1.53 ± 0.10 $x10^{-3}$ mm^2/s). Another study by Fuji et al observed lower ADC values in endometrial carcinoma (0.98± 0.21 $x10^{-3}$ mm^2/s) and carcinosarcoma (0.97± 0.02 $x10^{-3}$ mm^2/s) compared with submucosal leiomyoma (1.37± 0.28 $x10^{-3}$ mm^2/s) and endometrial polyp (1.58± 0.45 $x10^{-3}$ mm^2/s). They also showed a cut off value for differentiation of malignant from benign lesions as 1.15 $x10^{-3}$ mm^2/s with a sensitivity of 84.6% and specificity of 100%. In the present study we observed ADC values for endometrial carcinoma as 1.85 $x10^{-3}$ mm^2/s for *b* 100, 1.16 $x10^{-3}$ mm^2/s for *b* 600, and 0.91 $x10^{-3}$ mm^2/s for *b* 1000.

Naganawa et al. observed lower ADC values in cervical cancer lesions compared with normal cervical tissue (1.09 ± 0.20 $x10^{-3}$ mm^2/s, vs, 1.79 ± 0.24 $x10^{-3}$ mm^2/s, $p<0.0001$) (10). Similarly, Chen et al. observed lower ADC values in cervical carcinoma compared with normal cervical tissue (1.110 ± 0.175 $x10^{-3}$ mm^2/s, vs, 1.593 ± 0.151 $x10^{-3}$ mm^2/s, $p<0.001$) (11). The study by Mcveigh et al. showed lower ADC values in cervical carcinomas compared with normal cervix (1.09 ± 0.20 $x10^{-3}$ mm^2/s, vs, 2.09 ± 0.46 $x10^{-3}$ mm^2/s, $p<0.001$) (12). In the present study, we observed ADC values for cervical carcinoma as $2.14x10^{-3}$ mm^2/s for *b* 100, $1.18x10^{-3}$ mm^2/s for *b* 600 and $0.86x10^{-3}$ mm^2/s for *b* 1000.

There are various studies that investigate the value of DWI in differentiating ovarian lesion in the literature. Nakayama et al. observed lower ADC values in mature cystic teratomas compared with other benign and malignant ovarian cystic masses ($p<0.005$) (16). Moteki et al. observed lower ADC values in endometrial cyst and malignant ovarian tumors compared with ovarian cyst, serous cystadenomas and mucinous cystadenomas ($p<0.02$) (17). Another study by Moteki et al. showed lower ADC values in cystic contents of endometrial cysts and malignant cystic ovarian tumors compared with ovarian cysts and serous cystadenomas ($p<0.003$) (18). Bakır et al. investigated the usefulness of DWI in solid or predominantly solid adnexial and ovarian lesions, and observed no significant difference between malignant and benign masses' ADC values (5). Zhang et al. observed a significantly lower mean ADC value of the solid component of malignant tumors compared with benign tumors ($p<0.05$) (6). Another study by Zhang et al. observed lower ADC values in malignant adnexial tumors compared with benign ones ($p=0.000$) (7).

A study by Namimoto et al. reviewed the role of DWI in the diagnosis of gynecological diseases and concluded that ADC can help to differentiate malignant from normal tissue in the uterin cervix and endometrium (19). They also added the utility of this technique is limited in uterine myometrium and ovaries. In the present study we evaluated the accuracy of DWI in differentiation of malignant versus benign gynecologic lesions. We observed significantly lower ADC values in malignant lesions in all *b* values ($p= 0.047$ for *b* 100, $p<0.001$ for *b* 600, $p<0.001$ for *b* 1000). We also evaluated the cut-off points of ADC value for the differentiation of malignant from benign lesions and observed $1.6x10^{-3}$ mm^2/s for *b* 100 with a sensitivity of 40% and a specificity of 88%; $1.4x10^{-3}$ mm^2/s for *b* 600 with a

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sensitivity of 57% and a specificity of 77%, and $0.9x10^{-3}$ mm^2/s for *b* 1000 with a sensitivity of 57% and a specificity of 91%. According to these analyses, ADC value at *b* 1000 was found to have the highest accuracy for differentiation of malignant from benign gynecologic masses.

There are some limitations in this study. The total cohort has a sufficient sample size; however, subgroup size is quite small. The lesions included in this study have heterogeneity such as being cystic or solid. However, our purpose was to differentiate malignant lesions from benign ones, independent of lesions' nature and other imaging findings.

In conclusion, we observed significantly lower ADC values in gynecologic malignant lesions in all *b* values with the highest accuracy for ADC value at *b* 1000. According to our study, ADC measurements can be used for differentiation of malignant from benign gynecologic lesions.

Conflict of interest: The authors declare that they have no conflict of interest

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