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Diffusion-Weighted Imaging of Solid Ovarian Masses: Is it Useful to Differentiate Benign From Malignant?

Solid Over Kitlelerinde Difüzyon Ağırlıklı Görüntüleme: Benign-Malign Ayrımında Faydalı Mı?

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ÖZ

Amaç: Apparent diffusion coefficient (ADC) değerlerinin benign-malign solid over kitlelerinin ayrımında faydalı olup olmadığını araştırmak.

Araçlar ve Yöntem: Çalışmamıza geriye dönük olarak 50 hastanın 62 solid over kitlesi dahil edildi. Hastalar benign ve malign olmak üzere 2 gruba ayrıldı. On üç hastanın 13 over kitlesi benign tanı alırken, 37 hastanın 49 over kitlesi malign tanı aldı. Lezyon boyutları ve solid over kitlelerinin ADC değerlerinin karşılaştırılmasında Mann-Whitney U testi kullanıldı. Malign-benign ayrımında bir cut-off ADC değeri hesaplamak için receiver-operating characteristic (ROC) eğrisi kullanıldı.

Bulgular: Gruplar arasında yaş (p=0.06), tüm lezyon boyutu (p= 0.647) ve solid komponent boyutu (p=0.066) arasında istatistiksel anlamlı farklılık yoktu. İki grup arasında ADC değerlerinde anlamlı farklılık saptandı (p=0.015). ADC değerleri istatistiksel anlamlı olarak malign grupta daha düşüktü. ROC analizi ile eğri altında kalan alan 0.722 ve cut-off ADC değeri 0.886 x 10^{-3} mm^2/s olarak hesaplandı.

Sonuç: Difüzyon ağırlıklı görüntüleme solid over kitlelerinin ayırıcı tanısında kullanışlı bir tekniktir. Solid over kitlelerinde düşük ADC değerleri benign lezyondan ziyade malign bir lezyona işaret etmektedir.

Anahtar Kelimeler: apparent diffusion coefficient; difüzyon ağırlıklı görüntüleme; solid over kitlesi

ABSTRACT

Purpose: To research whether apparent diffusion coefficient (ADC) values of solid ovarian masses are beneficial for differentiation between benign and malignant.

Materials and Methods: We analyzed 50 patients with 62 solid ovarian masses retrospectively. We divided the ovarian masses into two groups as benign and malignant. Thirteen patients with 13 solid ovarian masses were identified to have benign masses, while 37 patients with 49 solid ovarian masses were diagnosed with malignancy. The Mann-Whitney U test was used for the comparisons of the sizes and the ADC values of solid ovarian mass. Receiver-operating characteristic (ROC) curves were analyzed to determine a cut-off value for ADC to differentiate benign from malignant.

Results: No significant differences were found between the two groups in terms of age (p=0.06), whole lesion size (p= 0.647), and solid component size (p=0.066). ADC values of the two groups were significantly different (p=0.015). Malignant solid ovarian lesions showed significantly lower ADC values than benign lesions. The ROC curves showed an area under the curve rate of 0.722 and a cutoff value of 886 x 10^{-6} mm^2/s.

Conclusion: Diffusion-weighted imaging is a useful method for differential diagnosis of solid ovarian masses. Lower ADC values of solid ovarian lesions indicate malignancy rather than benign lesions.

Key Words: apparent diffusion coefficient; diffusion-weighted imaging; solid ovarian mass

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INTRODUCTION

Ovarian masses, including benign and malignant, are a prominent cause of gynecological surgeries. Ovarian malignancies are the most common cause of death in gynecological cancers and fifth in cancer-related deaths in women.[1] Clinical course of ovarian malignancies is usually silent. Therefore, the majority of ovarian cancer patients present in the end-stage of the disease. Imaging methods are essential in the detection, characterization and staging of ovarian masses. Ultrasound (US) and magnetic resonance imaging (MRI) are the widely adopted diagnostic methods to diagnose ovarian masses. The main goal of imaging is making a distinction between malignancies and benign lesions and to guide clinicians in patient management.[2] The sensitivity of the US is high; however, its specificity is low. On the other hand, MRI with higher soft tissues resolution and advantages of multidimensional imaging is the best diagnostic tool for the characterization of ovarian masses. Some useful MRI findings have been reported to differentiate between benign and malignant lesions.[3] Lesion size, septal and wall thickness, internal papillary projections, nodularity, enhanced solid portions, hemorrhage, and necrosis are some of them, and are widely discussed in the literature.[4] However, these imaging parameters have been found to overlap for benign and malignant ovarian lesions. Based on these results, differential diagnosis of ovarian masses by conventional MRI examination is still challenging for radiologists.[4] Recently, in addition to conventional MRI, functional MRI techniques like diffusion-weighted imaging (DWI) have been used to improve the diagnostic accuracy of MRI for ovarian masses.[5]

DWI is a new and functional MRI technique that reflects the motion of water molecules. The movement of water molecules in tissues is interrupted by intra-extracellular structures such as membranes, matrix fibers, and macromolecules. Apparent diffusion coefficient (ADC) is a measurable and quantitative water diffusion data in body tissues. A lower signal on ADC maps and a higher signal on DWI show restricted diffusion and are associated with hypercellularity or malignancy.[6] Therefore, ADC values can be helpful in the characterization of solid ovarian masses. There are several studies investigating the efficacy of DWI in the differentiation of benign ovarian lesions from malignant ones; however, controversial results have been reported.[2,4,5,7-12]

We aimed to investigate whether DWI and ADC values may prove useful in making a distinction between benign and malignant ovarian lesions.

MATERIALS and METHODS

Patients

We retrospectively analyzed 67 patients with solid ovarian masses who underwent pelvic MRI in our radiology department between January 2018 and June 2020. The inclusion criteria were as follows: 1- surgical and pathologically confirmed solid ovarian masses, and 2- no history of treatment for ovarian lesions before pelvic MRI. The exclusion criteria were as follows: 1- MRI from another center (n=11), 2- heavy image artefacts (n=3), and 3- lack of DWI sequences (n=3) (Figure 1).

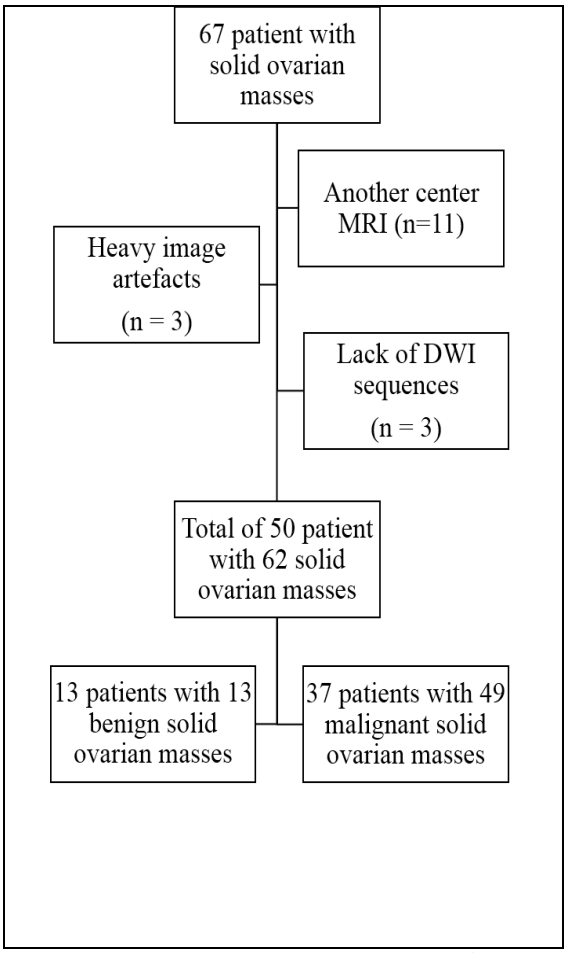

Figure 1. Diagram shows the study exclusion criteria of the study.

A total of 50 patients with 62 solid ovarian masses were included in our study. Patients were divided into two groups as benign solid ovarian mass (Group 1) and borderline or malignant ovarian mass (Group 2). We also excluded the mature cystic teratomas since these lesions were easy to diagnose by conventional MRI and did not pose a diagnostic challenge. The collected clinical information is shown in Table 1. Our institutional ethical committee approved the study protocol (decision number:13/267, date:23.07.2020).

MRI Protocol

MRI was performed using a 1.5 T system (Siemens, Avanto, Erlangen, Germany). Turbo spin echo (TSE) T2W coronal (TR/TE, 4450/108; NEX, 1; the FOV of 450 mm; 4 mm section thickness), T2W axial TSE (TR/TE, 5190/108; NEX, 1; the FOV of 420 mm; 5 mm thickness), TSE T2W sagittal (TR/TE, 4290/108; NEX, 1; the FOV of 280 mm; 4.5 mm section thickness) and TSE T1W axial (TR/TE, 716/10; NEX, 1; the FOV of 420 mm; 5 mm section thickness) sequences were performed. DWI was performed at b-values of 50, 400 and 800 s/mm^2 (TR/TE, 6600/81; NEX, 2; FOV 420 mm; slice thickness 5 mm). Pre- and post-contrast fat-saturated TSE T1-weighted axial (TR/TE, 716/10; NEX, 1; and the FOV of 420; 5 mm section thickness) sequences were performed. After IV contrast administration (gadolinium-diethylenetriamine pentaacetic acid, 0.1 mmol/kg intravenously at a rate of 1.5 mL/s), axial, sagittal and coronal plane T1W fat-saturated scans were performed.

Image Analysis

Magnetic resonance images of the solid ovarian masses were examined by an abdominal radiologist (MAG) who was blinded to the information about histopathological diagnosis and had more than 2 years of experience in gyneco-oncologic imaging. The sizes of the lesions were measured in 2 different ways. Firstly, each lesion was measured in the axial plane with its largest diameters. Secondly, the dominant solid components were measured in the axial plane with their largest diameters. All measurements were performed on contrast-enhanced T1W fat-saturated images separately. The ADC values of the solid component of the ovarian masses were then measured. Regions of interest (ROIs) were located in solid components of the ovarian mass on ADC maps on three different localization. To decide the contrast-enhanced part of the mass and to avoid the cystic-necrotic component of the lesion, T2W, DWI and contrast enhanced fat-saturated T1 weighted images were used as a reference (Figure 2, 3). The final ADC value of the ovarian masses was calculated by taking the average of the 3 different ROIs.

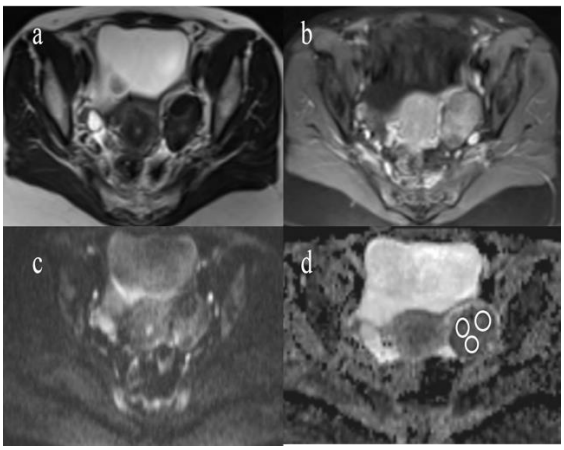

Figure 2. T2 weighted image (a), contrast-enhanced fat-saturated T1 weighted image (b), diffusion-weighted image (c), and apparent diffusion coefficient maps (d) of left ovarian fibroma. Image d shows the measurement of apparent diffusion coefficient value from 3 different contrast-enhanced solid areas.

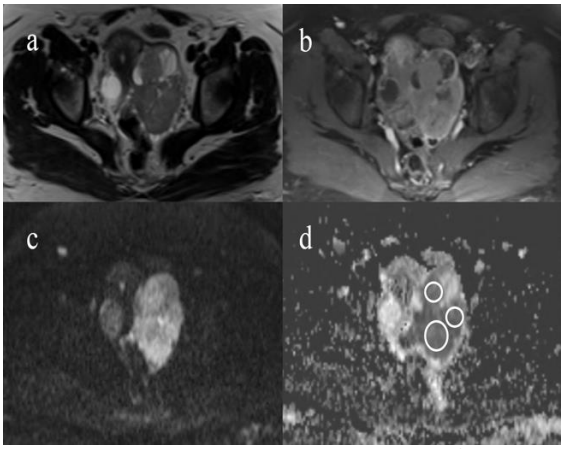

Figure 3. T2 weighted image (a), contrast-enhanced fat-saturated T1 weighted image (b), diffusion-weighted image (c), and apparent diffusion coefficient maps (d) of bilateral ovarian high-grade serous carcinoma. Image d shows the measurement of apparent diffusion coefficient value from 3 different contrast-enhanced solid areas.

Statistical Analysis

IBM SPSS Statistics 20.0 (Armonk, NY: IBM Corp.) statistical software was used in statistical analysis. The normality was tested using Kolmogorov-Smirnov test. Mean ± standard deviations were calculated. The Mann-

Whitney U test was used to compare the sizes of ovarian masses and the ADC values of enhanced solid ovarian mass in Group 1 and Group 2. For statistical significance, a p-value of less than 0.05 was considered. ROC curves were calculated to set a cut-off value for the diagnosis of solid ovarian masses in statistically significant parameters.

RESULTS

Thirteen patients (26% with mean age 42.1, range 20-76) with 13 solid ovarian masses were identified to have benign masses, while 37 patients (74% with mean age 48.2, range 20-61) with 49 solid ovarian masses were diagnosed with malignancy. In the malignant group, 25 patients had unilateral and 12 patients had bilateral ovarian masses. Benign solid ovarian lesions were diagnosed as follows: 6 fibromas, 5 fibrothecomas, 1 techoma, and 1 hemangioma. Malignant solid ovarian lesions were diagnosed as follows: 23 serous cystadenocarcinomas, 10 borderline cystadenocarcinomas, 4 mucinous cystadenocarcinomas, 5 Krukenberg tumors (4 from gastric cancer and 1 from colorectal origin), 2 clear-cell carcinomas, 2 granulosa cell tumors, 1 endometrioid adenocarcinoma, 1 malignant Brenner tumor, and 1 malignant mixed germ cell tumor. No statistically significant differences were detected between benign and malignant ovarian masses in terms of age (p=0.06), whole lesion size (p=0.647), solid component size (p=0.066). ADC values were significantly different between the two groups (p=0.015). ADC values of malignant ovarian masses were significantly lower than benign ones ($1.024\pm0.397\ 10^{-3}\ mm^2/s$ vs $1.273\pm0.338\ 10^{-3}\ mm^2/s$). The mentioned results are summarized in Table 1.

Table 1. Baseline patient characteristics of the benign and malignant ovarian lesions

Characteristics	Benign ovarian mass (13 patients with 13 lesions)	Malignant ovarian mass (37 patients with 49 lesions)	P value
Age (years) mean±SD, median (min-max)	42.1±9.6, 42 (20-61)	48.2±14.6, 48 (20-76)	0.06
Size of whole lesions (mm) mean±SD, median (min-max)	75.7±57.3, 61 (26-240)	75±46.7, 62(25-263)	0.647
Size of solid component (mm) mean±SD, median (min-max)	65.3±31.4, 61(26-120)	47.5±21.1, 44 (11-107)	0.066
ADC x 10-3 mm2/s (mean±SD), median (min-max)	1.273±0.338, 1226(0.889-2.042)	1.024±0.397, 0.945(0.516-2.484)	0.015

ADC= apparent diffusion coefficient

The ROC curve analysis revealed the diagnostic accuracy for ADC (area under the curve (AUC)=0.722, p=0.0012). The AUC rate revealed that the ADC values were statistically significant to differente benign from malignant. The collected data are presented in Table 2 and Figure 4.

Table 2. Sensitivity, specificity, positive predictive and negative predictive values of apparent diffusion coefficient in making benign-malignant distinction of solid ovarian lesions with receiver operating characteristic curve analysis.

Predictive Values	Cut-off value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC	p values
ADCx10-3 mm2/s	>0.886	100	42.6	32.5	100	0.722	0.0012

ADC= apparent diffusion coefficient

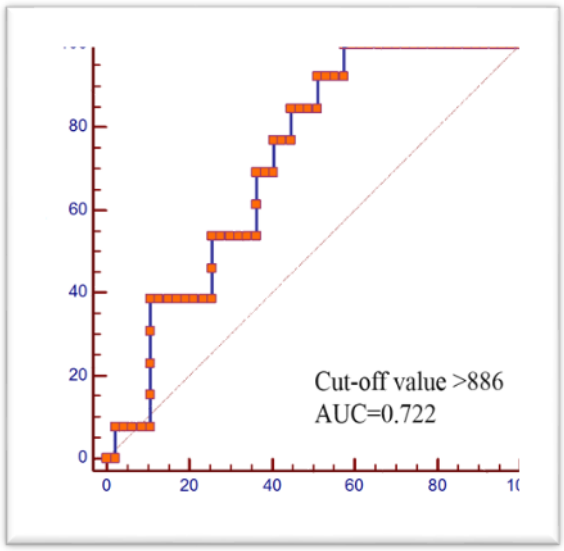

Figure 4. Receiver operating characteristic curves of apparent diffusion coefficient value.

DISCUSSION

The current study showed that ADC values of solid ovarian masses were useful in distinguishing between benign and malignant lesions. Malignant solid ovarian masses had higher ADC values than benign solid lesions. There are numerous studies investigating the usability of DWI for the differential diagnosis of ovarian masses. However, the results are largely contradictory: some studies have suggested that DWI is effective to differentiate between benign and malignant ovarian lesions[4,5,8,9], while others have shown inconsistent results.[10-12]

Takeuchi et al.[8] used ADC values to discriminate benign from malignant ovarian tumors and reported similar results to ours. The mean ADC value of benign ovarian tumors measured by Takeuchi et al.[8] was $1.38x10^{-3}$ mm^2/s, while malignant tumors was $1.03x10^{-3}$ mm^2/s. In the present study with larger sample size, the mean ADC value of benign ovarian lesions was $1.27x10^{-3}$ mm^2/s, while the mean ADC value of malignant lesions was $1.02x10^{-3}$ mm^2/s. In another study, which supports our results, Wang et al.[9] investigated DWI for benign-malignant differentiation in epithelial tumors and demonstrated the ADC values of $0.86x10^{-3}$ mm^2/s for malignant tumors and $1.28x10^{-3}$ mm^2/s for benign epithelial ovarian lesions[9]. In another similar study, Li et al.[4] investigated epithelial ovarian lesions and presented a cut-off ADC value of $1.25x10^{-3}$ mm^2/s. [4] Turkoglu and Kayan showed the efficacy of DWI in benign-malignant ovarian mass differentiation and demonstrated a cut-off ADC value of $0.93x10^{-3}$ mm^2/s with an AUC rate of 0.724.[5] In the present study, we found a cut-off ADC value of $0.886x10^{-3}$ mm^2/s with an AUC rate of 0.722. The ADC values of solid ovarian masses in our study were lower than those found by the studies of Li[4] and Turkoglu and Kayan.[5] The differences in ADC values between studies may be associated with selected b-values or imaging parameters, ROI placement techniques, and histopathological types of tumors. We are of the opinion that the lower ADC values of malignant ovarian masses may be associated with increased cellularity, vascularity, and aggressive behavior of malignant lesions.

On the other hand, Fujii et al.[10], Bakir et al.[11], and Kierans et al.[12] investigated benign and malignant adnexal masses and showed no significant differences in ADC values of solid components. They thought that this overlap for ADC values of benign and malignant ovarian lesions may be associated with interstitial edema and desmoplastic stroma in malignant lesions. Additionally, these different results may be related to different patient selection methods. Moreover, these studies also included mature cystic teratomas and endometriomas.[10,12] These types of lesions show lower ADC values which overlap with malignant masses and may result in a reduction in the diagnostic efficiency of DWI. The lower ADC values of teratomas have been associated with the keratinoid content of these masses. On the other hand, the abnormal signal intensity of endometriomas on DWI is associated with high concentrations of blood and hemosiderin, which has been shown in nearly half of the endometriomas.[2] In addition, endometriomas and mature cystic teratomas are easily diagnosed by conventional MRI sequences in most cases, and there is no need for DWI. When teratomas and endometriomas are excluded, as in our study, the diagnostic performance of DWI will increase. Fujii et al.[10] and Kierans et al.[12] included mature cystic teratomas and endometriomas as benign ovarian lesions, which may explain why there were no significant differences between malignant and benign ovarian lesions. However, Bakir et al.[11] did not include teratomas and endometriomas. Kierans et al.[12] also conducted an analysis by excluding endometriomas and teratomas, and the ADC values of

other benign ovarian masses continued to show no significant difference. This highlights the hypothesis that desmoplastic stroma and interstitial edema may cause high ADC values in malignant lesions. But these two studies were limited with small sample sizes.

Some studies have shown that the mean age at which adnexal masses are seen is not a significant variable for the differentiation of benignity and malignancy.[4,5,13] In the present study, similar to previous studies, there were no significant differences between the mean ages of the two groups. On the other hand, the size of the lesion is also not a useful variable to distinguish benign from malignant ovarian lesions.[6,13] In the present study, not only the sizes of the whole lesion but also the sizes of the dominant solid components were not helpful in the distinction of benign and malignant lesions.

The current study has several limitations. The first one was the small sample size and the design of the study, which was retrospective. Secondly, the majority of the benign group consisted of fibroma and fibrothecoma. We aimed to evaluate solid or dominantly solid ovarian masses; therefore, we excluded the lesions with no measurable solid components. Thirdly, a manual ROI placement technique was used. Manual ROI placement technique may bias the study results, which is a widespread problem for all of the ROI-based studies.

In conclusion, DWI with ADC measurements seems to be a useful method for the differentiation of benign solid ovarian masses from malignant ovarian tumors. ADC values of solid ovarian masses can be an important element of diagnostic radiology in a daily practical approach.

Conflict of Interest

The authors declare that there is not any conflict of interest regarding the publication of this manuscript.

Authors' Contributions

Concept/Design: MAG. Data Collection and/or Processing: MAG. Data analysis and interpretation: MAG. Literature Search: MAG. Drafting manuscript: MAG. Critical revision of manuscript: MAG. Supervision: MAG.

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