# Role of Diffusion Weighted MRI in Characterization of Ovarian Tumors

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## ABSTRACT

**Background:** Ovarian masses present a special diagnostic challenge when imaging findings cannot be categorized into benign or malignant pathology. Ultrasound (US), computed tomography (CT) and magnetic resonance imaging (MRI) are currently used to evaluate ovarian tumors. Functional imaging by means of diffusion weighted magnetic resonance imaging (DW-MRI) is now part of the standard imaging protocols for evaluation of the female pelvis. DW-MRI is important MR imaging technique which enable the radiologist to move from morphological to functional assessment of diseases of the female pelvis.
**Aim of the Study:** The aim of the current study is to evaluate the diffusion-weighted MR imaging in prediction of the nature of suspicious ovarian masses which are detected previously by conventional ultrasound.
**Patients and Methods:** MRI Unit, radiodiagnosis department, Ain Shams University hospital. The study is prospective, included thirty women who presented with suspicious adnexal masses on previous ultrasound examination and referred for further assessment and characterization by DW-MRI. Patients with contraindications to MRI (e.g. claustrophobia, cardiac prosthesis and metallic plates) are excluded.
**Results:** The study included 30 women ranging in age between 24 and 61 years with mean age 43.22±11.15. Out of 30 cases, 12 had of benign ovarian tumors while 18 had malignant tumors.
**Conclusion:** Thus, combination of DWI and conventional MRI implies using a completely noninvasive technique with no radiation exposure. It is cost effective (no additional cost to MRI examination), and easily added to the MR study protocols with no marked lengthening of examination time. It improves the specificity of MRI and thus increasing radiologist's confidence in image interpretation which will finally reflect on patient's outcome and prognosis.
**Keywords:** Diffusion weighted, MRI, CT, US, Ovarian tumors.

## INTRODUCTION

Ovarian masses present a special diagnostic challenge when imaging findings cannot be categorized into benign or malignant pathology. Ultrasound (US), computed tomography (CT) and magnetic resonance imaging (MRI) are currently used to evaluate ovarian tumors **(1).** Ultrasound is the first- line imaging investigation for suspected adnexal masses helping in detection and characterization of ovarian tumors (1). Computed tomography is commonly performed for evaluation of a suspected ovarian malignancy, but it exposes patients to radiation (2).

Magnetic resonance image can be a valuable problem solving tool, an adjunctive modality for evaluating adnexal lesions, useful to give also surgical planning information without radiation exposure **(3).**

MRI is able to identify different types of tissue contained in pelvic masses, distinguishing benign from malignant ovarian tumors, with an overall accuracy of 88% to 93% (2). However, the only definitive diagnosis of an ovarian mass is through histology **(3).**

Recent technical advances allow the use of dynamic and diffusion MR imaging in abdominal and pelvic applications **(4).**

Functional imaging by means of diffusion weighted magnetic resonance imaging (DW-MRI) is now part of the standard imaging protocols for evaluation of the female pelvis. DW-MRI is important MR imaging technique which enable the radiologist to move from morphological to functional assessment of diseases of the female pelvis **(5).**

In general, malignant tumors have a higher cellularity than benign tumors; therefore, DWI can assist in differentiating malignant from benign tumors **(6).**

Diffusion-weighted MR imaging is used for tumor detection, tumor characterization, and the evaluation of treatment response in patients with cancer **(7).**

When diffusion-weighted MR imaging is used in gynecologic applications, cancers have shown lower ADC (apparent diffusion coefficient) values **(8).**

## AIM OF THE STUDY

The aim of the current study is to evaluate the diffusion-weighted MR imaging in prediction of the nature of suspicious ovarian masses which are detected previously by conventional ultrasound.



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## PATIENTS AND METHODS

**Study setting**

MRI Unit, radiodiagnosis department, Ain Shams University hospital.

**Study Population**

The study is prospective, included thirty women who presented with suspicious adnexal masses on previous ultrasound examination and referred for further assessment and characterization by DW-MRI. Patients with contraindications to MRI (e.g. claustrophobia, cardiac prosthesis and metallic plates) are excluded.

## METHODS

MR imaging was performed on a 1.5-Tesla MRI machine (Achieva, Philips medical system). All patients were imaged in the supine position using pelvic phased-array Torso coil.

**The patients were subjected to:**

- Full clinical assessment.
- Revision of the patient's laboratory investigations as tumor marker.
- Revision of the radiological investigations previously done for the patients.
- Checking for contraindication to MRI imaging (e.g. pacemaker, metallic implant, and severe claustrophobia).
- Informed consent was taken from all patients before MR imaging.

**Patient preparation**

- Administration of an antispasmodic drug (10 mg of visceralgine) was given immediately before MR imaging to reduce bowel peristalsis.
- Fasting for 6 hours before post contrast MRI imaging.

**MR imaging protocol:**

- Axial T1-weighted (TR/TE, 500/10 ms) and axial T2-weighted (TR/TE, 3300/100 ms), slice thickness, 6 mm. Gap, 1 mm. FOV, 32–42 cm. Matrix, 256 × 256.
- Sagittal T2-weighted and Coronal T2-weighted, Slice thickness, 8–10 mm. Gap, 1 mm. FOV, 40–50 cm. Matrix, 256 × 256.
- DW-MRI was acquired in the axial plane by using a single shot echo-planar imaging sequence with b values (0, 300, 600). TR/TE, 5000/70. Slice thickness, 6 mm. Gap, 1 mm. FOV, and 36 cm. Matrix, 128 × 128.
- Post contrast T1WI (axial and coronal) after injection of 0.1 mmol/kg body weight of Gd-DTPA.

**MR images analyzed for the following:**

- The morphological features of each lesion will be recorded including size, border, signal characteristics at T1 and T2 and enhancement.
- Signal intensity on diffusion images with measurement of ADC values.
- Histopathological examination was done for all patients and the results were correlated with imaging findings of DW-MRI.

The study was approved by the Ethics Board of Ain Shams University.

### *Statistical methods*

IBM SPSS statistics (V. 24.0, IBM Corp., USA, 2016) was used for data analysis. Date were expressed as Mean±SD for quantitative parametric measures in addition to both number and percentage for categorized data.

**The following tests were done:**

1. Comparison between two independent mean groups for parametric data using Student t test.
2. Chi-square test to study the association between each 2 variables or comparison between 2 independent groups as regards the categorized data. The probability of error at 0.05 was considered sig., while at 0.01 and 0.001 are highly sig.
3. Diagnostic validity test: It includes:

a. The diagnostic sensitivity: It is the percentage of diseased cases truly diagnosed (TP) among total diseased cases (TP+FN).

b. The diagnostic specificity: It is the percentage of non-diseased truly excluded by the test (TN) among total non-diseased cases (TN+FP).

c. The predictive value for a +ve test: It is the percentage of cases truly diagnosed among total positive cases.

d. The predictive value for a -ve test: It is the percentage of cases truly negative among total negative cases.

e. The efficacy or the diagnostic accuracy of the test: It is the percentage of cases truly diseased plus truly non-diseased among total cases.

## RESULTS

The study included 30 women ranging in age between 24 and 61 years with mean age 43.22±11.15.

Out of 30 cases, 12 had of benign ovarian tumors while 18 had malignant tumors. The histopathological types of benign tumors included: 2 mature teratoma (6.7%), 2 tubo-ovarian abscess (6.7%), 1 fibrothecoma (3.3%), 2 serous cystadenofibroma (6.7%), 2 endomaterioma (6.7%) and 3 serous cystadenoma (10.0%), while the malignant tumors included: 6 serous cystadenocarcinoma (20.0%), 4 mucinous cystadenocarcinoma (13.3%), 3 granullosa cell tumor (10.0%), 3 immature teratoma (10.0%) and 2 dysgerminoma (6.7%), **(Table 5-1)**.

**Table (5-1):** Histo-Pathological types of ovarian tumors in the study group.

| Pathological type | | |
|---|---|---|
| **Benign** | **12** | |
| Fibrothecoma | 1 | 3.3% |
| Endometrioma | 2 | 6.7% |
| Mature teratoma | 2 | 6.7% |
| Serous cystadenofibroma | 2 | 6.7% |
| Tubo-ovarian abscess | 2 | 6.7% |
| Serous cystadenoma | 3 | 10.0% |
| **Malignant** | **18** | |
| Dysgerminoma | 2 | 6.7% |
| Granullosa cell tumor | 3 | 10.0% |
| Immature teratomas | 3 | 10.0% |
| Mucinous adenocarcinoma | 4 | 13.3% |
| Serous cystadenocarcinoma | 6 | 20.0% |

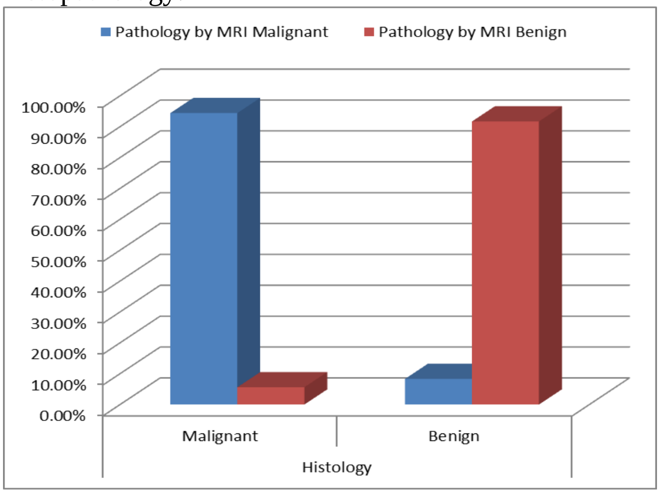
According to the MRI findings, among the 30 cases, 18 diagnosed to be malignant and 12 diagnosed to be benign, however, comparison to histopathology **(Figure 5-1)** revealed:

**17 cases (True +ve)** showed typical criteria of malignant lesions by MRI and proved to be malignant by histopathology.

**1 case (False +ve)** suspected to be malignant by MRI was proved to be benign by histopathology**.**

**11 cases (True –ve)** showed typical criteria of benign lesions by MRI, and proved to be benign by histopathology.

**1 case (False –ve)** suspected to be benign by MRI was proved to be malignant by histopathology.

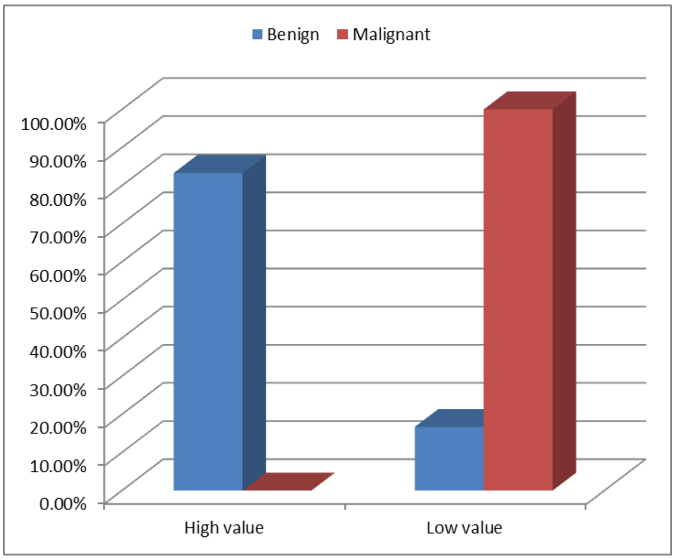



**(Figure 5-1):** Comparison between MRI and histopathology.

Correlation between histological results and MRI results showed 94.4% Sensitivity (ability to detect malignant) ; 91.7% Specificity (ability to detect benign); 91.7%; NPV (ability of detect TN among all negative results) ; 94.4% PPV (ability of detect TP among all positive results) and 93.3% accuracy (ability to detect TN+TP among all cases), with p value < 0.05 denoting statistical significance with 93.3% agreement.

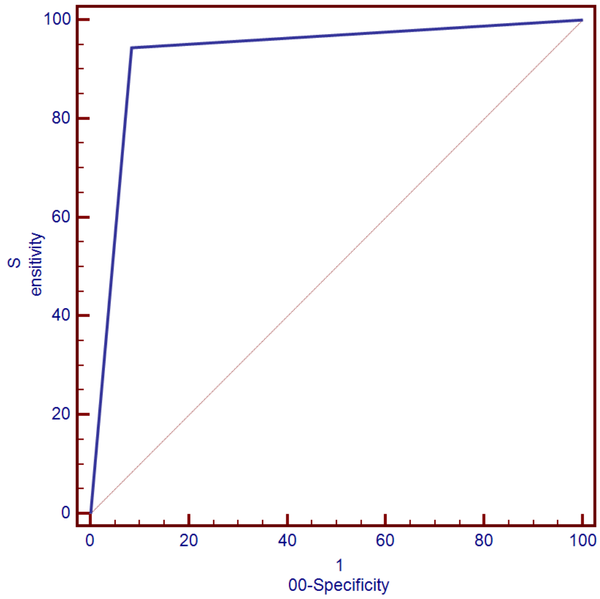
The patients ADC value in cases with benign tumors ranged from 0.8 to 1.39 (mean ADC value $1.22 \pm 0.20 \times 10^{-3}$). While the ADC value in cases with malignant tumors; ranged from 0.71 to 0.91 ADC value (mean ADC value $0.82 \pm 0.07 \times 10^{-3}$) with p-value <0.001 denoting high statistical significance.

All malignant as well as two benign ovarian lesions (tubo-ovarian abscess) showed diffusion restriction with low ADC value, while the rest of benign tumors showed no diffusion restriction with high ADC value **(Figure 5-2).**




**(Figure 5-2):** Bar chart compared between benign and malignant tumors according to ADC value.

In our study we can define the best cut off value of ADC which was 0.91, with sensitivity of 94.4% specificity of 91.7% positive predictive value of 94.4 %, negative predictive value of 91.7% and diagnostic accuracy of 93.3 % on Receiver-operating characteristic curve **(Figure 5-3).**

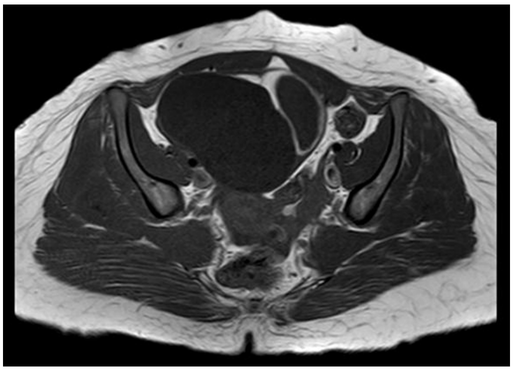



**(Figure 5-3):** Receiver-operating characteristic (ROC) curve analysis showing the diagnostic performance of ADC values for discriminating patients with benign from those malignant ovarian tumors.

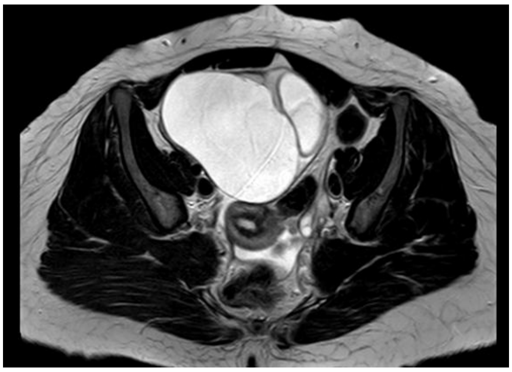
Illustrative Cases:

**CASE 1:**

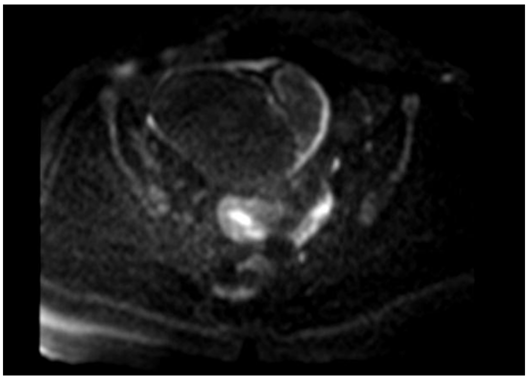
24 years old female patient, single, presented with lower abdominal pain. Pelvic ultrasound showed right ovarian cyst measuring 8×10×13 cm.



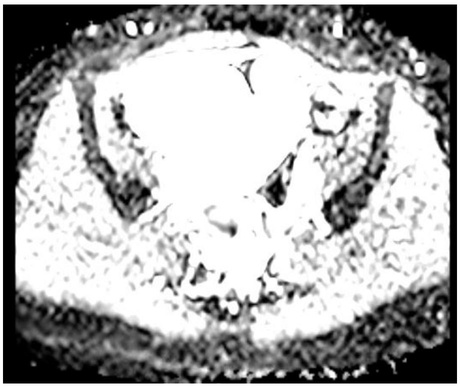
T1 WI



T2 WI



DWI



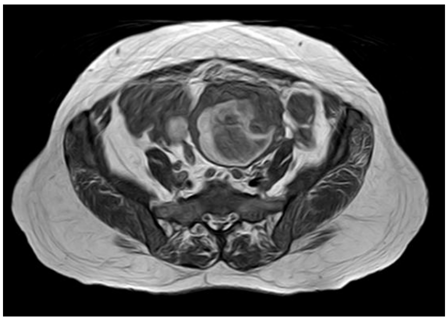
ADC map

Right adnexa shows a well-defined relatively large cystic lesion measuring about 8.7 x 12.7 x 13 cm extending to mid line. It is seen biloculated displaying hypointense signal on T1WI and hyperintense signal on T2WI. No diffusion restriction on DWI with increase ADC value (1.19×10-3 mm2/sec.).

Suggestive diagnosis: ovarian serous cystadenoma (Approved by histopathology).

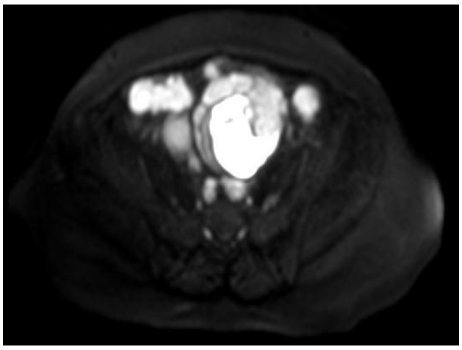
**CASE 2**

53 years old female patient sent to MRI due to hetrogenous pelvic mass in lower abdomen detected by US 6.7×8×8.5 cm.

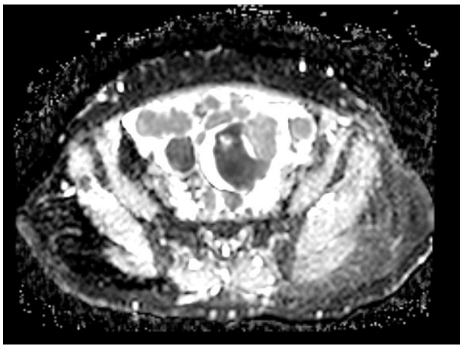


Axial T1 WI

Axial T2 WI



DWI



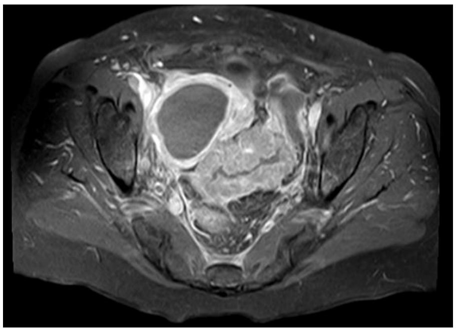
ADC map

Left adenxal complex solid and cystic mass lesion is noted measuring 8.2 x 8.3 x 9 cm.
The cystic component shows intermediate T1 WI signal and high T2 WI signal.
The solid component shows hypotense T1 WI signal, isotense T2 WI signal, high signal on DWI and low signal on ADC map with low ADC value that means true diffusion restriction (ADC value =0.71x10-3mm2/sec.). Multiple peritoneal deposits are noted that also show true diffusion restriction.

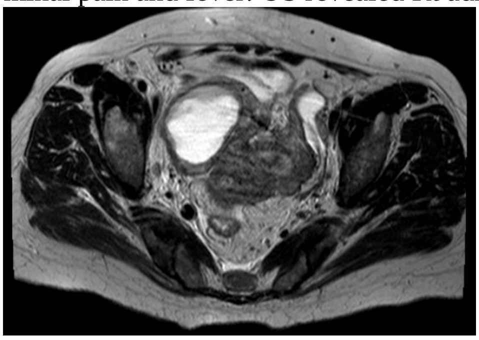
The findings are suggestive malignant ovarian mass (histopathologicaly proven to be mucinous cystadenocarcinoma) with peritoneal deposits.

**CASE 3**

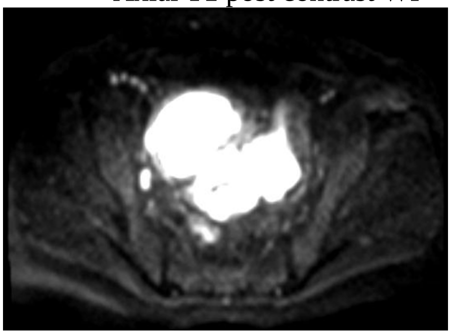
46 years old female patient presented with lower abdominal pain and fever. US revealed Rt adnexal cyst.



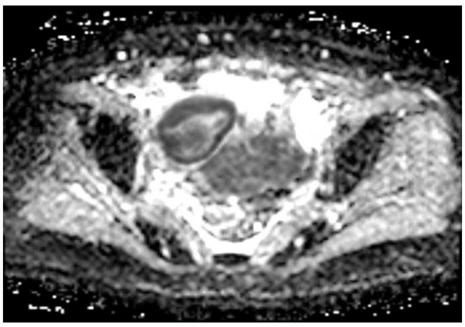
Axial T1 post contrast WI



Axial T2 WI



DWI



ADC map

The right adnexa shows a well defined cystic lesion measuring about 5.7 x 6.7 cm in maximum dimensions. It displays hypointense signal with peripheral enhancement on post-contrast T1WI, hyperintense signal on T2 WI. On

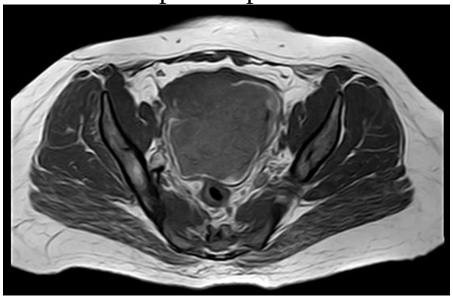
DWI the lesion shows high signal intensity with low ADC value that means true diffusion restriction. (ADC value=0.84×10-3mm/sec.)

Suggestive diagnosis: Right adnexal tubo-ovarian abscess (Approved by histopathology)

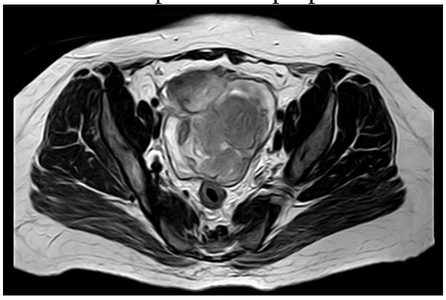
**N.B:** The uterus also shows the same signal characterizes, denoting its involvement by the implanting process.

**CASE 4:**

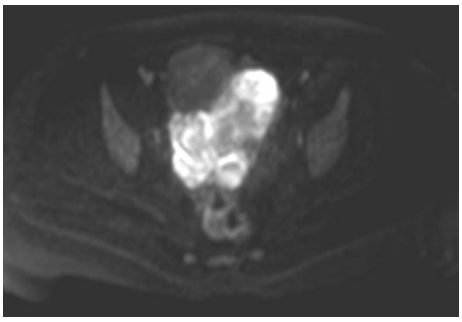
47 years old female patient presented with lower abdominal pain with palpable mass.



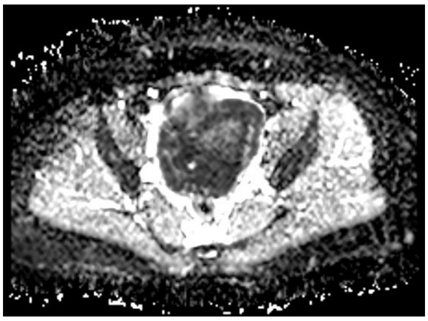
T1 WI



Axial T2 WI



DWI



ADC map

A large left adenexal heterogeneous lesion, 9.6x 9.9x 13.3cm, with iso-intense signal on T1 WI and hetrogenous signal on T2 WI. On DWI the lesion appears heterogeneous with areas of high signal and low ADC value that means true diffusion restriction.(ADC value=0.78×10-3mm2/sec.).

The findings are suggestive of malignant of ovarian neoplasm (histopathologicaly proven to be immature teratoma).

**DISCUSSION**

Ovarian cancer is a leading cause of death among women. It is the second most common gynecological cancer and the fifth most common cancer in women. Unfortunately most women are diagnosed with late stage disease, which has a poor survival rate. Proper diagnosis of cancer can help finding more available treatment options and in turn better prognosis [(9)]**.**

MR imaging has shown to be more specific and accurate than US and Doppler assessment in characterizing adnexal masses. In addition, it is the best method in delineation of local spread to the pelvic organs [(10)]**.**

**DWI** is one of the promising new functional imaging techniques. As long as interpretation of DWI is combined with the conventional MR images and with realizing of the possible pitfalls, it has shown to be effective in the differentiation of benign from malignant adnexal masses [(11)]**.**

In this study, among the examined thirty cases with ovarian masses, 12 were benign ovarian tumors and 18 cases were malignant ovarian tumors. The mean ADC values for malignant lesions was (0.82×10$^{-}$3mm$^2$/s) while that for benign lesions was (1.22× $10^{-3}$ mm$^2$/s), with cutoff point (0.91×$10^{-3}$) and p value < 0.05 which was considered of statistical significance. The sensitivity was 94.4%, the specificity was 91.7%, and the accuracy was 93.3%.

Some benign ovarian tumors (tubo-ovarian abscess) showed high signal intensity on DWI with low ADC values which is the same characteristic of malignant tumors. While the other benign tumors showed low or intermediate signal on DWI with low ADC values.

A study was carried out by **Koyama *et al.*** [(12)] on 35women to determine the accuracy of DWI imaging in the characterization of ovarian masses in patients undergoing pelvic MRI. The study included 26 benign tumors, 8 malignant tumors and 1 borderline tumor. Malignant lesions only showed definite high signal intensity in DW images. DWI has specificity of 85% which is relatively comparable to our study where the specificity was 91.7%. In their study the sensitivity was 100%. In our study, there were two false positive cases while in their study they excluded the teratomas and haemorragic cysts.

Another study was conducted by **Fujii and colleagues** [(6)] on 123 ovarian lesions including 42 malignant and 81 benign lesions, most malignant ovarian tumors as well as some of the mature cystic teratomas showed high signal intensity on **DWI**. In contrast, most benign tumors did not show abnormal high signal intensity on DWI. This agree with our results that all the malignant lesions (8 cases ) and 2 tubo-ovarian abscess showed high signal on DWI, this may be attributed to restricted substances in abscess.

Our study also matched with another study carried out by **Li and colleagues** [(13)] on 127 patients with pelvic masses, (46 benign and 85 malignant). The purpose of this study was to evaluate differences in ADC values for the solid component of benign and malignant ovarian surface epithelial tumors with the goal of differentiating benign versus malignant ovarian tumors preoperatively.

The **mean ADC value** measured for the **solid** component was significantly differed between the benign and malignant lesions. **Mean ADC value** for **benign lesions** was$1.69\times10^{-3}\pm0.25$ SD $mm^2/s$, and for the **malignant** was $1.03\times10^{-3}\pm0.22$SD $mm^2/s$. The lower ADC values associated with the malignant group were found to be statistically significant. Their results suggest that an ADC value$\geq 1.25 \times 10^{-3}$ $mm^2/s$ may be an optimal cutoff value for differentiating benign and malignant ovarian tumors.

A similar study was carried out by **Takeuchi and colleagues** [(14)] on 47 women (33malignant, 6 borderline, and 10 benign tumors). The **mean (SD) ADC** value in malignant tumors $1.03\times10^{-3}$ $mm^2/s$ was significantly lower than that in the 10 benign tumors $1.38\times10^{-3}$ $mm^2/s$., using a cutoff ADC value of **1.15**, with sensitivity, specificity, PPV, NPV and accuracy of 96.5%, 89.1%, 94.3%, 93.2%, and 93.1%.

This was relatively comparable to our study where the mean ADC values for malignant lesions was ($0.82\times10^{-}3mm^2/s$) while that for benign lesions was ($1.22\times 10^{-3}$ $mm^2/s$), with cutoff point ($0.91\times10^{-3}$) , showing sensitivity, specificity, PPV, NPV and accuracy were 94.4%, 91.7%, 93.3%, 91.7% and 93.3% respectively.

Small number of patients in the study group is a limiting factor. So, further studies with large number of patients and wider range of histological types of ovarian lesions are recommended.

## SUMMARY AND CONCLUSION

Although the final diagnosis of an ovarian tumor is based on the histological examination, it is desirable to preoperatively differentiate between benign, border line tumors and invasive ovarian cancers, in order to decide if surgery is required, and which type of surgery is appropriate. Thus, it can help avoiding unnecessary surgery especially in postmenopausal women and help deciding for conservative surgery for young ones wishing to preserve childbearing potential.

Conventional MRI provides soft tissue characterization based on different signal intensities and contrast uptake in post contrast images.

Being a cost effective choice, and in addition to its ability for accurate diagnosis, it can replace computed tomography (CT) in preoperative assessment with the development of recent technologies, new functional MRI sequences are being used. Of these, is the diffusion weighted images (DWI) and dynamic contrast enhanced MRI (DCE-MRI). DWI is used in the abdomen and pelvis after it has been established as a useful functional imaging tool in neurologic applications for a number of years.

DWI depends on the fact that water molecules can diffuse freely in low cellular environment, while tissue hyper cellularity causes its restriction, a phenomenon called '**Brownian motion'**. As a result, malignant ovarian tumors due to their hyper cellular nature show restriction of diffusion, unlike most benign tumors. So it implies a noninvasive technique which can be used especially if contrast intake is avoided as in pregnancy.

Our study which was conducted on thirty ovarian masses showed that DWI is more in specificity and accuracy than conventional MRI.

In this review, we present the development of diffusion analysis to characterize sonographically indeterminate adnexal masses, using ADC values and visual assessment of DW signal, functional criteria help the radiologist to improve lesion characterization especially for benign lesions and should help the clinician to avoid unnecessary surgeries. The mean ADC values for benign lesions was ($1.22\times 10^{-3}$ $mm^2/s$), while for malignant lesions was ($0.82\times10^{-}3mm^2/s$) with cutoff point ( $0.91\times10^{-3}$ ). The sensitivity was 94.4%, the specificity was 91.7%, and the accuracy was 93.3%.

Thus, combination of DWI and conventional MRI implies using a completely noninvasive technique with no radiation exposure. It is cost effective (no additional cost to MRI examination), and easily added to the MR study protocols with no marked lengthening of examination time. It improves the specificity of MRI and thus increasing radiologist's confidence in image interpretation which will finally reflect on patient's outcome and prognosis.

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