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Diffusion Magnetic Resonance Imaging in Differentiation of Ovarian Cystic Lesions

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: MRI can specifically diagnose some certain pathologic types by providing accurate information on fat, collagen and hemorrhage. Diffusion-weighted magnetic resonance imaging, an emerging non-invasive MRI technique, is of the capability to evaluate the extent of microscopic diffusion which might exist in biologic tissues. Evidence has shown that DWI-MRI and ADC were beneficial in differentiating malignant from benign ovarian lesions and may be helpful to predict suboptimal cytoreduction in ovarian cancer. The aim of this study to assess the role of magnetic resonance imaging with diffusion weighted images in the assessment and differentiation of ovarian cystic lesions.
Methods: This prospective study was conducted on 30 female patients who are proved by ultrasound to have ovarian cystic lesions. Selected patients were given butylscopolamine bromide (20mg) administered IV or intramuscularly at the beginning of the examination. Imaging is performed with the patient in the supine position with an empty urinary bladder. A distended urinary bladder is not recommended because it increases phase ghost artifacts and can compress the uterus.

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Results: As regards diagnosis according to Ultrasound examination, revealed that ovarian cancer and simple cyst were the most frequent (26.7% and 20% respectively), followed by Tubo-ovarian hydrosalpinx and Hemorrhagic cyst (10%) each. Ovarian serous cyst adenoma constituted (6.7%), while pyosalpinx, PCO, hydrosalpinx, and endometrial cyst constitutes (3.3%) each.
As regards diagnosis according to MRI examination, Simple cyst and ovarian cancer were the most frequent (13.3%) each, followed by Tubo-ovarian hydrosalpinx and Hemorrhagic cyst (10%) each. Krekenberg tumor, Ovarian dermoid, and Ovarian serous cyst adenoma constituted 6.7% each. As regards the ADC value was significantly lower in the malignant lesions ($0.7*10^3$) than benign ones ($0.9*10^3$). As regards histopathologic confirmation, 23 cases of the studied women, Ovarian cancer (17.4%), Tubo-ovarian hydrosalpinx (13.0%), and Hemorrhagic cyst (13.0%) were the most common diagnosis. Ovarian dermoid, Krekenberg tumor, and Ovarian serous cyst adenoma constituted 8.7% each. Other less frequent diagnosis included Endometeriotic cyst, Hydrosalpnix, Mucinous cystadenoma, Ovarian serous cyst adenocarcinoma, Ovarian dysgerminoma and Terato-dermoid (4.3%) each. The mean ADC value was significantly lower in the malignant lesions than benign ones. At a cut off ≤0.7, ADC showed a significant good diagnostic value of malignant lesions with sensitivity, Specificity, and an accuracy.
Conclusions: DWI to conventional MRI is an important tool. It improves the specificity of MRI and thus increasing radiologist's confidence in image interpretation which will finally reflect on patients'outcome and prognosis. Cost effective technique (no additional cost to MRI examination), was easily added to MR study protocols.

Keywords: Diffusion; MRI; differentiation; ovarian cystic lesions.

1. INTRODUCTION

The ovarian cystic lesions are group including endometrioma, benign cystic teratoma, hemorrhagic, cystadenoma, and Malignant lesions [1].

MRI is useful for definitively diagnosing many common benign adnexal lesions. MRI better characterizes indeterminate adnexal lesions seen on ultrasound, especially if an extraovarian cystic lesion is suspected but a normal ipsilateral ovary is not seen and if a predominantly solid lesion requires more tissue-specific characterization for diagnosis. Finally, MRI is a valuable tool in characterizing a complex cystic ovarian mass as an endometrioma and may detect signs of relatively rare malignant degeneration within it [2].

MRI can specifically diagnose some certain pathologic types by providing accurate information on fat, collagen and hemorrhage. Diffusion-weighted magnetic resonance imaging, an emerging non-invasive MRI technique, is of the capability to evaluate the extent of microscopic diffusion which might exist in biologic tissues. Typically, DW-MRI permits a quantitative evaluation by assessing apparent diffusion coefficient values which measures the random motion rate of water molecules and decreases with increased tumor cellularity. It is useful in the diagnosis of gynecologic tumors has been reported in several studies. DW-MRI has been considered as an effective tool to characterize epithelial ovarian tumors through helping discriminate benign, borderline and invasive tumors. Evidence has shown that DWI-MRI and ADC were beneficial in differentiating malignant from benign ovarian lesions and may be helpful to predict suboptimal cytoreduction in ovarian cancer [3].

Diffusion-weighted imaging is a non-contrast MRI technique increasingly used in abdominal and pelvic imaging. Optimized ultrafast echo-planar imaging techniques for body applications along with parallel imaging, higher gradient amplitudes, and high density phased-array surface coils, have enabled routine use of DWI in many abdominopelvic MRI protocols [4].

The aim of this study to assess the role of magnetic resonance imaging with diffusion weighted images in the assessment and differentiation of ovarian cystic lesions.

2. PATIENTS AND METHODS

The present study was prospective one that was conducted on 30 patients that are proved by ultrasound to have ovarian cystic lesions and referred to Radiodiagnosis Department of Tanta University Hospitals from the Obstetrics and Gynecology Department of Tanta University Hospitals and outpatient clinics.

2.1 Inclusion Criteria

Female patients with sonographic findings of ovarian cysts. No age predilection.

2.2 Exclusion Criteria

- Patients known to have contraindications for MRI, e.g. an implanted magnetic device, pacemakers or claustrophobia.
- Patients with bad general condition needing life support and those with severe hepato-renal disease.
- Impaired renal function.
- Purely solid ovarian masses.

2.3 Patient Preparation and Methods

- Before MRI, patients are typically instructed to fast for 4-6 hours to diminish artifacts due to small-bowel peristalsis.
- In addition, an antiperistaltic agent, such as butylscopolamine bromide, (dose 20mg) is administered IV or intramuscularly at the beginning of the examination.
- Imaging is performed with the patient in the supine position with an empty urinary bladder. A distended urinary bladder is not recommended because it increases phase ghost artifacts and can compress the uterus.

2.4 Careful Clinical History Taking

Age, sex, history of any systemic disease and history of any malignancy.

- Clinical examination: abdominal and pelvic examinations of the patient.
- laboratory investigations: including C.B.C and renal function tests (serum creatinine).
- Histopathology: 23 cases were underwent histopathologic confirmation.
- Ultrasound examination(using siemens device):

  - Using convex probe.
  - Using transvaginal probe (in virgin: transvaginal probe was not be used).

- MRI examination:

Using a 1.5 tesla MRI scanner [general electric (GE) Medical Systems].

- The sequences of each MRI study were:
  - T1-weighted image (TR<800, TE<30, flip angle: 90 degrees).
  - T2-weighted image (TR>2000, TE>80, flip angle: 90 degrees).
  - T1W sequence with fat saturation after administration of Gadolinium in lesions proved by US to have solid component, as they may help differentiate solid components or papillary projections from clots and debris.
- Diffusion Weighted (DW) MR Sequence.

2.5 Statistical Analysis

Data were collected, tabulated, statistically analyzed using a personal computer with Statistical Package of Social Science (SPSS), where the following statistics were applied. Quantitative data were presented as median and IQR and were compared by Mann-Whitney test. Qualitative data were presented as frequency and percent and were compared by Chi-square test. ROC curve was used to determine cut off of ADC value. A two-tailed P value <0.05 was considered statistically significant.

3. RESULTS

This study included 30 female patients; their age's ranged from 6.0-60.0 years with a mean of 31.9±10.4. The most frequent age group was less than 30 years followed by 30<40 (40% and 36.7% respectively). The majority (86.7%) of patients were married. There were 29 patients (96.7%) did not receive hormonal therapy. There were 15 patients (50%) reported history of pelvic pain, followed by vaginal bleeding (23.3%) Table 1.

Ultrasound examination revealed that ovarian cancer and simple cyst were the most frequent (26.7% and 20% respectively), followed by Tubo-ovarian hydrosalpinx and Hemorrhagic cyst (10%) each. Ovarian serous cyst adenoma constituted 6.7%, while pyosalpinx, PCO, hydrosalpinx, and endometrial cyst constitutes 3.3% each Table 2.

Simple cyst and ovarian cancer were the most frequent (13.3%) each, followed by Tubo-ovarian hydrosalpinx and Hemorrhagic cyst (10%) each. Krekenberg tumor, Ovarian dermoid, and Ovarian serous cyst adenoma constituted 6.7% each Table 3.

Table 1. Patient characteristics of the studied patients (n=30)

		N	%
Age groups	<30	12	40.0%
	30<40	11	36.7%
	40-60	7	23.3%
Marital status	Married	26	86.7%
	Not married	4	13.3%
Hormonal therapy	No	29	96.7%
	yes	1	3.3%
Clinical history	Pelvic pain	15	50.0%
	Vaginal bleeding	7	23.3%
	Abdominal enlargement	4	13.3%
	Abdominal pain	3	10.0%
	Pelvic pain &abnormal vaginal bleeding	1	3.3%

Table 2. Diagnosis of the ovarian lesions according to the ultrasound examination

		N	%
US	Complex solid and cystic lesions	8	26.7%
	Well defined anechoic cyst with no septations	5	20.0%
	Bilateral cystic lesions with septation and clear content.	4	13.3%
	Adnexal cystic lesion with lace-like reticular echoes.	3	10.0%
	Cystic adnexal mass with echogenic components	3	10.0%
	Adnexal cystic lesion contain thin septations	2	6.7%
	Bilateral cystic lesions with internal turbid content	1	3.3%
	Bilateral polycystic peripheral located follicle	1	3.3%
	Adnexal cystic lesion with acoustic enhancement with diffuse homogeneous ground-glass echoes.	1	3.3%
	Anechoic adnexal lesion less than 3cm	1	3.3%

Table 3. Diagnosis according to MRI

		N	%
MRI	Simple cyst	4	13.3%
	Papillary serous cystadenocarcinoma	4	13.3%
	Tubo-ovarian hydrosalpnix	4	13.3%
	Hemorrhagic cyst	3	10.0%
	Krekenberg tumor	2	6.7%
	Ovarian dermoid	3	10%
	Ovarian serous cyst adenoma	2	6.7%
	Tubo-ovarian pyosalpnix	1	3.3%
	Polycystic ovaries	1	3.3%
	Ovarian dysgerminoma	1	3.3%
	Endometriotic adenocarcinoma	1	3.3%
	Mucinous cystadenoma	1	3.3%
	Gartner duct cyst	1	3.3%
	Follicular cyst	1	3.3%
	Endometeriotic cyst	1	3.3%

Ovarian cancer (17.4%), Tubo-ovarian hydrosalpinx (13.0%), and Hemorrhagic cyst (13.0%) were the most common diagnosis. Ovarian dermoid, Krekenberg tumor, and Ovarian serous cyst adenoma constituted 8.7% each. Other less frequent diagnosis included Endometeriotic cyst, Hydrosalpnix, Mucinous cystadenoma, Ovarian serous cyst adenocarcinoma, Ovarian dysgerminoma and Terato-dermoid (4.3%) each. Out of the studied women, 23 cases underwent histopathologic confirmation Table 4.

There were a statistically significant association between the nature of tumor whether benign or malignant and the diffusion restriction (p=0.034). Table 5.

The mean ADC value was significantly lower in the malignant lesions ($0.7*10^3$) than benign ones ($0.9*10^3$)(p=0.040) as demonstrated in Table 6.

At a cut off ≤0.7, ADC showed a significant good diagnostic value of malignant lesions (P = 0.021) with sensitivity, Specificity, and an accuracy of 62.5%, 77.27%, and 76.67% respectively Fig. 1.

Examples of cases are shown in Fig. 2 and Fig. 3.

4. DISCUSSION

In our study, the mean of ADC value for solid malignant lesions was ≤0.7, ADC showed a significant good diagnostic value of malignant lesions with sensitivity, Specificity, and an accuracy of 62.5%, 77.27%, and 76.67% respectively, with p-value =0.021.

Accurate characterization of ovarian lesion as being benign can avoid unnecessary surgery especially in post-menopausal women [5]. Proper management depends on proper preoperative assessment, with the help of clinical examination, and different imaging modalities. Thus, helping to inform the patient about the surgical route and the possibility of conservative treatment [6].

Ultrasound is the primary imaging technique for adnexal lesions. MRI offers a great help in preoperative assessment of malignant masses, mainly with suspicious US criteria. MRI has emerged as an anatomical and functional imaging method that offers diagnostic accuracy in determining the origin and nature of ovarian lesions. This includes T2-weighted (T2-W) [7].

Diffusion-weighted imaging is a non-contrast MRI technique increasingly used in abdominal and pelvic imaging. Optimized ultrafast echo-planar imaging techniques for body applications along with parallel imaging, higher gradient amplitudes, and high density phased-array surface coils, have enabled routine use of DWI in many abdominopelvic MRI protocols [4].

Thomassin- Naggara et al. in [8] evaluated the contribution of DWI in conjunction with morphological criteria to characterize 77 complex adnexal masses (30benign and 47 malignant). According to them, low signal intensity on T2-weighted images and disappearance of restricted diffusion in the solid component may predict benignity.

Table 4. Diagnosis according to pathology

		N=23	%
Pathology	Papillary serous cystadenocarcinoma	4	17.4%
	Tubo-ovarian hydrosalpnix	4	17.3%
	Hemorrhagic cyst	3	13.0%
	Ovarian dermoid	3	13%
	Krekenberg tumor	2	8.7%
	Ovarian serous cyst adenoma	2	8.7%
	Endometeriotic cyst	1	4.3%
	Mucinous cystadenoma	1	4.3%
	Endometriotic adenocarcinoma	1	4.3%
	Ovarian dysgerminoma	1	4.3%

Table 5. Diffusion weighted in benign and malignant lesions

		Diffusion								Pathology	
		Free diffusion		Intermediate diffusion		Restricted diffusion					
		N	%	N	%	N	%	X^2	P value		N
Lesions	Benign	10	100.0%	1	33.3%	11	64.7%	6.73	0.034*	Benign	22
	Malignant	0	0.0%	2	66.7%	6	35.3%			Malignant	8
	Total	10	100.0%	3	100.0%	17	100.0%			Total	30

**significant at p<0.05*

Table 6. Mean ADC value in benign and malignant lesions

		Type of Lesions			
		Benign =22	**Malignant =8**	**z**	**P value**
Mean ADC value	Minimum	$0.6*10^3$	$0.5*10^3$	2.055	0.040*
	Maximum	$2.0*10^3$	$1.2*10^3$		
	Median	$0.9*10^3$	$0.7*10^3$		
	IQR	0.8-1.2	0.6-0.9		
	Mean rank	17.48	10.06		

**significant at p<0.05*

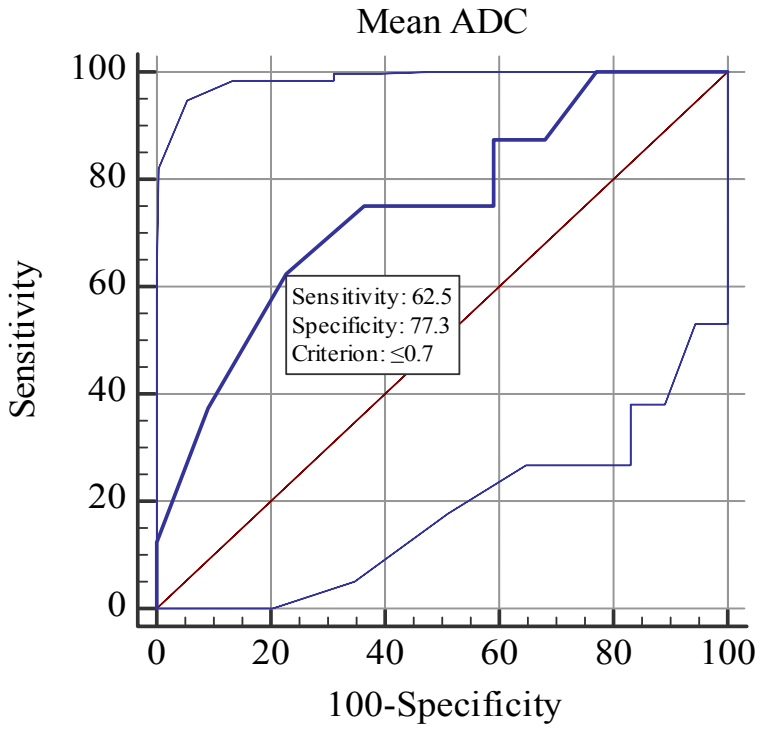

Fig. 1. ROC curve to determine cut off of ADC value

A similar study was carried out by Takeuchi et al in [9] on 49 ovarian tumors (39 malignant /borderline malignant, and 10 benign), it stated that the solid portions of all the 39 malignant tumors showed homogenous or heterogenous high intensity on DWI, whereas only 3 of the 10 benign tumors (3 thecomas)showed high intensity, the mean ADC value in the 39 malignant tumors $1.03x10^{-3}$ mm^2/s and was significantly lower than that of 10 benign tumors $1.38x10^{-3}$, they concluded that low DWI and high ADC intensity may may suggest benign lesion, however it may occasionally difficult to differentiate benign and malignant lesions only the basis of DWI. Such suggestion agrees with our study that showed that abundant cellular lesions (mature cystic teratoma, endometrioma& tubo-ovarian abscess,) showed high restricted diffusion.

Another study was carried out by Li, et al. [10] on 131 patients with pelvic masses,(46 benign and 85 malignant). The purpose of the study was to evaluate differences in ADC values for the solid component of benign and malignant ovarian surface epithelial tumors to differentiate benign from malignant tumors preoperatively. The mean ADC value measured for the cystic component did not differ significantly between benign and malignant masses. Unlike that measured for the solid component which significantly differed between the benign and malignant lesions. Mean ADC value for benign lesions was $1.69x10^{-3}$±0.25 SD mm^2/s, and for the malignant was

$1.03x10^{-3}$±0.22 SD mm^2/s. The lower ADC value associated with the malignant group was found to be statistically significant. Their results suggest that an ADC value ≥$1.25x10^{-3}$ mm^2/s an optimal cutoff value for differentiating benign and malignant ovarian lesions.

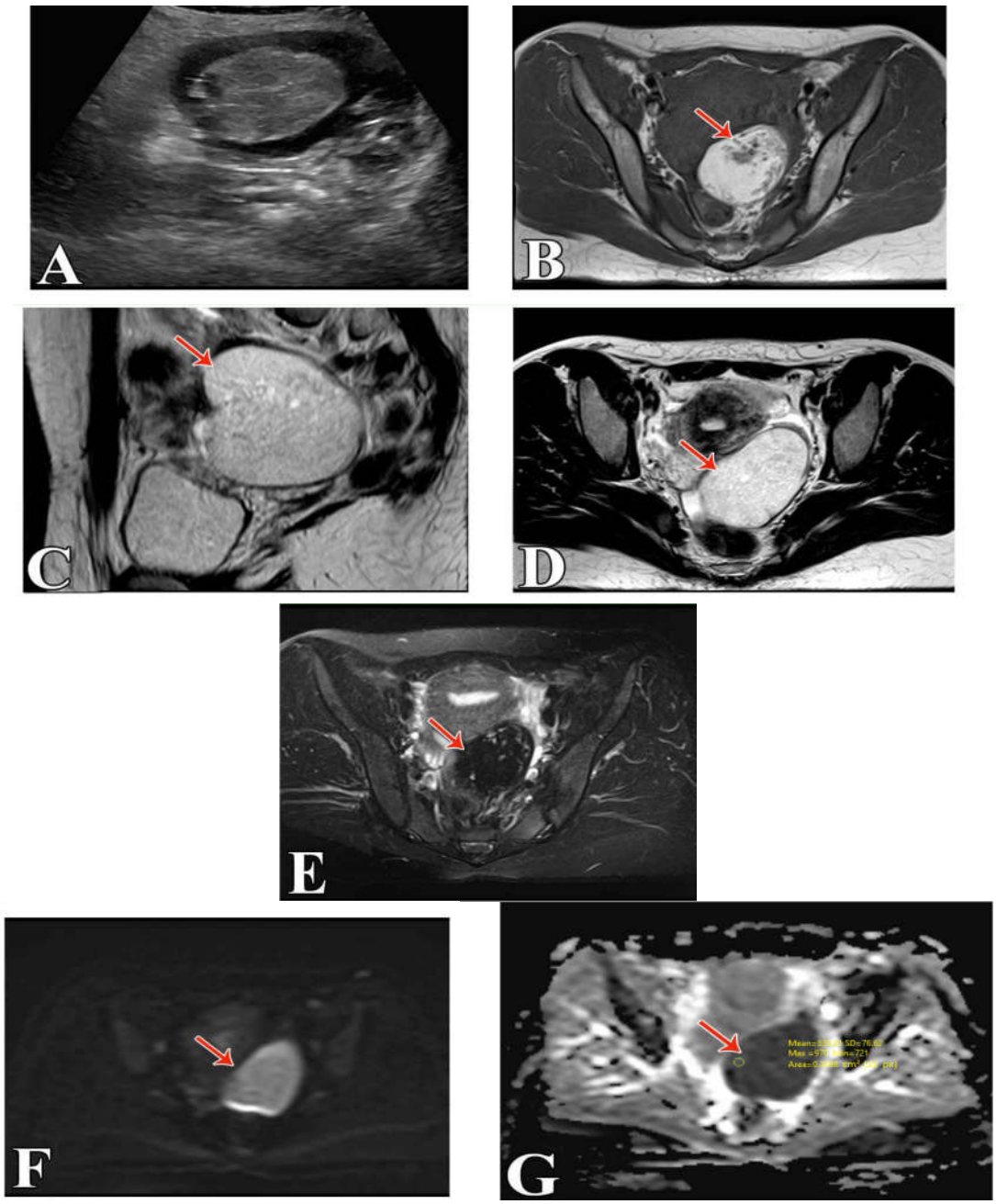

Fig. 2. 30-year-old woman presented with pelvic pain and was histologically proven to be Dermoid Cyst. a) Ultrasonography shows large left adnexal complex cystic lesion, B) axial T1 shows hyperintense left cystic ovarian cystic lesion. C & D: Sagittal and axial T2W1 shows hyperintense left cystic ovarian cystic lesion. E: AXIAL T2FATSAT shows left ovarian cystic lesion suppression at FATSAT denoting fatty content of the lesion F DWI shows restricted diffusion &G: mean ADC value of 0.8×10–3 mm2/s

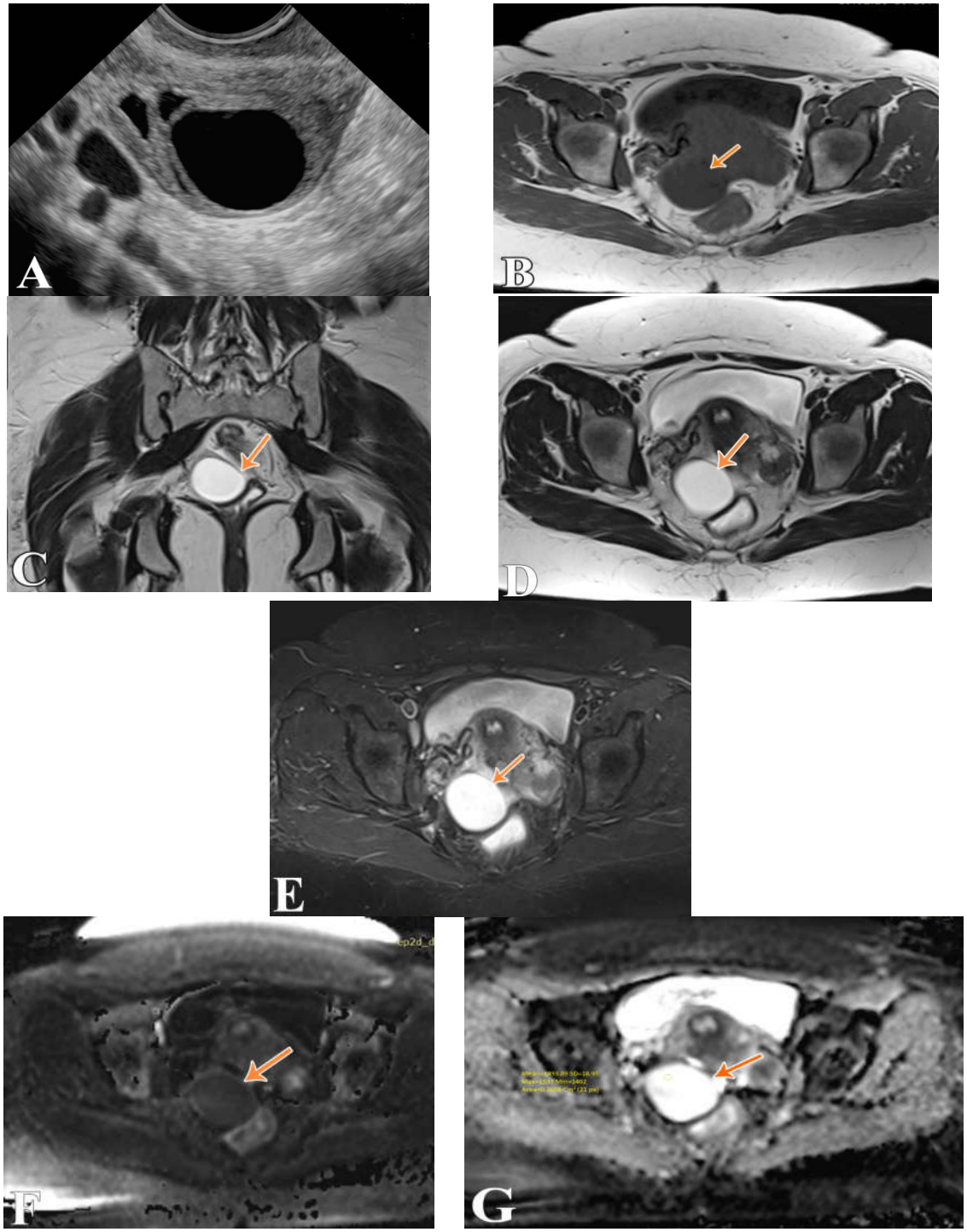

Fig. 3. 36 year old woman presented with pelvic pain and was histologically proven to be a case of simple cyst A: Ultrasonography shows right adnexal cyst with clear content, B: Axial T1 shows right adnexal hypointense lesion, C & D coronal and axial T2show hyperintense right adnexal cyst, E)Axial T2 STIR shows hyperintense right adnexal lesion, F) DWI shows free diffusion and G the mean ADC value of 1.5×10^{-3} mm^2/s

Also, Zhang P and colleagues in 2012 [11] performed another study on one hundred and 91 patients with 202 ovarian masses; 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 results of that study showed that DWI appears to be useful method for differentiating benign versus malignant ovarian tumors with solid components and malignant ovarian tumors, and is associated with high sensitivity and specificity, however, after exclusion of endometriomas, mature cystic teratoma and pure cystic adenoma from the analysis.

In more recent study Zhoa SH, et al. [12] to investigate diffusion weighted magnetic resonance (MR) imaging for differentiating borderline from malignant ovarian tumors of the ovary, the study included 60borderline epithelial ovarian tumors (BEOTs)in 48 patients and 65 malignant epithelial ovarian tumors (MEOTs)in 54 patients, results of the study showed, the majority of MEOTs to be of high signal intensity on DW imaging, where most of BEOTs showed low or moderate signal intensity. The mean of ADC value of the solid component of BEOTs ($1.562\pm0.346x10^{-3}mm^2/s$ was significantly higher than in MEOTs ($0.841\pm0.209x10^{-3}mm^2/s$.

Thomassin- Naggara et al. in [13] and Bouic-Pages et al. [14] also stated that the presence of vegetations or papillary projections suggested the diagnosis of borderline epithelial tumor and that their number and size are proportionally related to the tumor aggressiveness.

Lesion laterality and the fat saturation sequence showed statistically significant correlation regarding the cysts characterization. as agreed by Li et al. [15].

The current study found that the conventional MR features showed statistically high significant correlation in cystic ovarian lesion characterization. Similar findings were reported by Stevens et al. [16].

Nakayama et al. in [17] Hyun-Jung kim et al in [18] Bakir et al. in [19] and Fujii et al. [20] agreed to the current study regarding the DWI and ADC values as they reported that DWI and ADC value did not differentiate significantly between benign and malignant lesions with many overlaps between ADC values of both categories.

This overlap which was explained by Fujii et al. in [20] as it's due to increased mean ADC values in the malignant lesions and the decreased ADC values in benign lesions as the desmoplastic reaction in the stroma with cell packing may cause increased mean ADC values in malignant tumors. Nakayama et al. [17] also attributed the wide variation in the ADC values to the lesion morphological heterogeneity.

Thomasin-Naggara et al. [5] Sala et al. [21] & Feuerlein et al. [22] concluded that restricted diffusion is generally considered to be associated with malignant tumors because of the high cellularity of these tumors. However, in interpretation of diffusion-weighted images, it should be kept in mind that some of the benign lesions show degrees of restricted diffusion as a result of cell packing hindering free water molecules movement. For example, the high signal intensity on DWI and low signal intensity on the corresponding ADC maps may be due to restricted diffusion that also occur in areas of coagulative necrosis, abscesses, high mucin content or hemosiderin in a cystic lesion.

El Sorogy et al. [23] stated that determining the threshold of the ADC for diagnosing cystic ovarian tumors is difficult because of their large variance.

Contrarily, Zhang et al. [24] reported that there is statistically significant correlation in ADC value between benign and malignant lesions.

Accordingly, DWI and ADC maps are valuable sequences to be added to the routine pelvic MRI to help differentiate the benign from malignant lesions, not as an independent tool. Since then, several studies had analyzed the added value of DWI to conventional MRI protocol in order to differentiate benign from malignant adnexal/ ovarian tumors.

In the 30 studied cystic ovarian lesions the accuracy of DWI/ mean ADC value was 76.67%, sensitivity 62.5%, specificity 77.27%. Contrarily, Michielsen et al. [25], found higher accuracy of DWI/ADC map reaching to 91%.

5. CONCLUSIONS

DWI to conventional MRI is an important tool. It improves the specificity of MRI and thus increasing radiologist's confidence in image interpretation which will finally reflect on patients'outcome and prognosis. Cost effective

technique (no additional cost to MRI examination), was easily added to MR study protocols.

CONSENT AND ETHICAL APPROVAL

This study was done from May 2019 to May 2020 after approval from the Ethical Committee of Faculty of Medicine, Tanta University. An informed consent was obtained from all participants in this research after full explanation of the benefits and risks of the procedure.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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