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Original article

Dynamic Contrast-Enhanced and Diffusion Weighted Magnetic Resonance Imaging: Useful Tools for Characterization of Ovarian Masses

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Abstract

Background: Determining whether a clinically diagnosed adnexal mass is benign or malignant is frequently not possible until surgical exploration and histologic examination are performed. This study aimed at evaluating the role of diffusion-weighted MRI and dynamic contrast enhanced MR in characterization of ovarian masses. **Methods:** This prospective study included 40 patients, conducted in Radiology department in Benha University hospital .During the period from December 2020 to March 2022. The study protocol was approved by the Local Ethical Committee. **Results:** the addition of the DWI improved the sensitivity, PPV, NPV and accuracy of the conventional MRI from 74%, 76%, 44% and 66% to 89%, 78%, 64% and 75% respectively, yet the specificity was decreased from 47 % to 41 %. We had 12 borderline ovarian tumours which showed variable appearance on DWI. About ten cases showed facilitated diffusion of its solid component with a high ADC value (1.4 x10-3mm2/S) suggesting benign pathology (false negative). Two cases showed restricted diffusion with high signal on DWIs and mean ADC value of 0.8 x10-3mm2/S, 7 lesions out of 17 (41.2%) showed steady rise with no definite peak (type 1 curve), and the other ten lesions (58.8 %) showed rapid rise with a plateau. Moreover, some of the invasive malignant lesions 18 (66.6 %) showed initial rapid steep early enhancement. **Conclusion:** DCE and DWIs sequences are good supportive techniques to conventional MRI in the categorization of ovarian masses into benign, borderline and invasive malignant tumours.

Key words: Contrast enhanced ; Diffusion -Weighted ;MRI; Ovarian Masses

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 tumours [(1)].

Adnexal masses are the most common causes of indications for gynaecological surgery, but very few are malignant [(2)]. Therefore, preoperative characterization of adnexal masses is important because it may alter the treatment planning approach [(3)]. The differential diagnosis of ovarian masses is always challenging for the radiologists, but this task is now made easier due to new imaging techniques [(4)].

Imaging methods have an important role in the detection ,characterization and staging of ovarian masses.

Magnetic resonance imaging (MRI) is particularly preferred due to the high contrast of soft tissue. Recent technical advances allow the use of dynamic and diffusion MR imaging in abdominal and pelvic applications [(5)].

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 [(6)]. In general, malignant tumours have a higher cellularity than benign tumours; therefore, DWI can assist in differentiating malignant from benign tumours [(7)].DCE-MRI depends on the leakage of contrast agent from capillaries into the extravascular extracellular space, thus allowing quantitative analysis which reflects the blood flow and the vascular permeability [(8)]. DCE-MRI of ovarian tumours is recommended for accurate characterization of internal architecture, especially for delineation of necrosis, papillary projections, solid components, septations, and peritoneal implants [(9)].

This study aimed at evaluating the role of diffusion-weighted MRI and dynamic contrast enhanced MR in characterization of ovarian masses.

Patients and Methods

This prospective study included 40 patients, and was conducted in Radiology Department in Benha University hospital equipped with 1.5 tesla (MRI) magnets, during the period from December 2020 to March 2022. Before starting the research participants' consent and Benha University ethical committee approval were taken. This study was performed on 40 patients with 56 adnexal lesions. All patients were imaged in the

supine position using pelvic phased-array Torso coil.

Patient preparation:

Inclusion criteria:

- Patients presented by ovarian masses based on U/S study.

Exclusion Criteria:

1. MRI contraindications.

- Aneurysm clips.
- Any metallic fragments or foreign bodies.
- Coronary and peripheral artery stents.
- Aortic stent graft.
- Prosthetic heart valves.
- Vena Cava filters.
- Cardiac pacemaker.
- Implanted cardioverter defibrillator (ICD).
- Electronic implant or device e.g. Insulin pump or other infusion pump.
- Cochlear implant.
- Known claustrophobia.

2. Contraindications of DCE MRI

I. Absolute: Previous or pre-existing nephrogenic systemic fibrosis.

II. Relative :

- Previous anaphylactic reaction to gadolinium containing contrast agent.
- Patients with GFR below 30mL/min/1.73m2.
- Unstable renal impairment.
- Hepatorenal syndrome.
- Patients with chronic liver function impairment may have reduced muscle mass. This may make GFR estimation less accurate. Therefore GFR below 40mL/min/1.73m2 rather than 30mL/min/1.73m2 is suggested for safe administration of gadolinium.

All patients were subjected to:

Full history taking with a special emphasis on: age, parity menstrual history, past history of gynaecological troubles or operations, family history of similar gynaecological diseases, previous pelvi-abdominal US, TVUS and previous MRI. Laboratory investigations including renal and liver functions. Pregnancy test and radiological examinations including conventional MRI (axial T1&T2, sagittal and coronal T2), DWI MRI and DCE-MRI (post contrast T1 fat sat) were also done .

MR Imaging protocol

- **Axial T1-weighted** (TR/TE , 500/10 ms)

- **Axial T2-weighted**(TR/TE , 3300/100 ms)
- Slice thickness, 6 mm .Gap, 1 mm. FOV, 32–42 cm. Matrix, 256 x 256.
- **Sagittal T2-weighted** .
- **Coronal T2-weighted**
- Slice thickness, 8-10mm .Gap, 1 mm. FOV, 40–50 cm. Matrix, 256 x 256.
- **DW-MRI** was acquired in the axial plane prior to administration of contrast medium by using a single shot echo-planar imaging sequence.
- With b values (o, 300, 600). TR/TE, 5000/70. Slice thickness, 6 mm. Gap, 1 mm. FOV, 36 cm. matrix, 128x128
- **Dynamic contrast-enhanced MRI**: post contrast T1 fat satTHRIVE (High Resolution Isotropic Volume Examination) images were obtained immediately after manually injected gadolinium at a dose of 0.1 mmol/kg of body weight (maximum, 20 mL), this was followed by injection of 20 mL of normal saline flushing the tube. Images were obtained sequentially at 0,30,60,90 and 120 sec. Finally, transverse, sagittal and coronal T1-weighted gradient-echo images were acquired**.**

MR Imaging analysis:

MR images were analyzed for the following:

- MR appearance of the tumour; either cystic, solid or mixed.
- Involvement of one or both ovaries.
- Signal intensity of the tumour.
- Enhancement of the solid component if present.
- Wall thickness and regularity of the tumour and its enhancement.
- Presence of vegetations and septations, their enhancement pattern and their size.
- Presence of ascites.
- Presence of infiltrated pelvic or para aortic lymph nodes.
- Involvement of other pelvic organs.
- Presence of peritoneal and omental deposit.

Suggestive MRI signal for benign masses:

- Simple cystic tumours show low signal intensity in T1-weighted images and high signal intensity on T2-weighted images with no solid component.
- Complex benign looking masses: High signal intensity on T1WI is considered either fat or blood. On fat suppressed

images low signal is noted with fat while high signal is still noted in blood.

Malignant MR criteria according to [10]:

- Presence of wall thickness > 3mm.
- Solid vegetations more than 1cm.
- Thick septa > 3mm
- Areas of necrosis and breaking down.
- Signs of tumour spread for staging: enlarged lymph nodes , ascites, peritoneal and omental deposit

Post contrast images were used for the recognition of enhancement of the solid component, the tumor wall, septations and vegetations.

According to signal characteristics, important features for characterizing benign masses:

- Cystic tumours show low signal intensity in T1-weighted images and high signal intensity on T2-weighted images.
- Complex benign looking masses: High signal intensity on T1WI is considered either fat or blood. On fat suppressed images low signal is noted with fat while high signal is still noted in blood.
- Solid tumour with very low signal intensity in T2WI is characteristic to fibrous tumour (e.g. ovarian fibroma).

The statistical methods:

Data were statistically described in terms of mean ± standard deviation (± SD), and range, or frequencies (number of cases) and percentages when appropriate. Accuracy was represented using the terms sensitivity and specificity. All statistical calculations were done using computer program SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

Results:

Diagnosis according to conventional MRI findings:

Table, 1 shows that according to the percentage of conventional MRI diagnosis, 11 (19.7%) were benign, 7 (12.5%) were borderline and 38 (67.8%) were malignant.

Regarding conventional MRI-Radiology, the sensitivity of the MRI was 74%, specificity was 47%, PPV was 76%, NPV was 44% and accuracy was 66% **(Table, 2)**.

1- Qualitative assessment:

The signal intensity of the different ovarian lesions was assessed in DWI high b values (500, 1,000 and 1,500) and corresponding ADC maps and 70% of the lesions showed

restricted diffusion (hyper-intense signal in DWI and hypo-intense in ADC map), whereas 30% displayed facilitated diffusion.

We also found that 10 out of 17 benign lesions (58.8%) showed restricted diffusion while the remaining showed facilitated diffusion (41.2%), two of the borderline lesions (n=2, 16.6%) showed restricted diffusion , whereas all the malignant lesions (n=27, 100%) showed restricted diffusion **(Chart, 1)**.

2-Quantitative assessment (ADC values):

Table, 3 shows the ADC values within the solid lesion and solid components of mixed cystic/solid and predominantly cystic lesions.

Regarding Diffusion Weighted Imaging the sensitivity, PPV, NPV, accuracy and specificity were 89%, 78%, 64 %, 75% and 41% respectively **(Table, 4)**.

Case Presentation

Fig. 1:64-year-old female patient with past history of cystectomy for serous cystadenocarcinoma, complaining of abdominal pain. US revealed a bilateral multiple complex adnexal lesions.

Conventional MRI (a & b) showed bilateral adnexal complex masses with thick wall, eliciting heterogeneous low T1 and heterogeneous low T2 signal intensity with small areas of high signal intensity in T2. DWI (c & d): the pelvic mass showed restricted diffusion in the form of high signal on DWI with corresponding low signal on ADC map. ADC value was 0.65·10_3 mm2/s. DWI suggested malignant nature. DCE-MRI (e & f): the lesion showed heterogeneous intense enhancement and the curve shows the following criteria: rapid rising curve then plateau suggesting malignant character. MRI diagnosis (conventional, DWI and DCE-MRI) multiple bilateral complex malignant adnexal lesions. Pathology revealed bilateral malignant papillary serous cystadenocarcinoma

Fig 2:56-year-old female patient complaining of abdominal pain with past history of hysterectomy. US revealed a large left complex adnexal lesion.

Conventional MRI **(A& B)** showed large left adnexal complex cystic mass measuring 11x10x10cm showing thick walls and septae with solid mural projections, eliciting low T1 and heterogeneous low T2 signal intensity with small areas high signal intensity in T2. DWI **(C& D)**: The pelvic mass showed restricted diffusion in the form of high signal on DWI with corresponding low signal on ADC map. ADC value was 0.76· 10_3 mm2/s. DWI suggested malignant nature. DCE-MRI **(E& F)**: the lesion showed

heterogeneous enhancement of the nodule and thick walls and septae and the curve shows the following criteria: rising curve with plateau suggesting malignant character. MRI diagnosed (conventional, DWI and DCE-MRI) left complex malignant adnexal lesion. Pathology revealed clear cell carcinoma.

Table 1 : Radiological diagnosis by conventional MRI among the studied cases**.**

		No.	%
Conventional MRI Diagnosis	**Benign**	11	19.7
	borderline	7	12.5
	malignant	38	67.8

Table 2:Relation between pathological classification and Conventional MRI-Radiology.

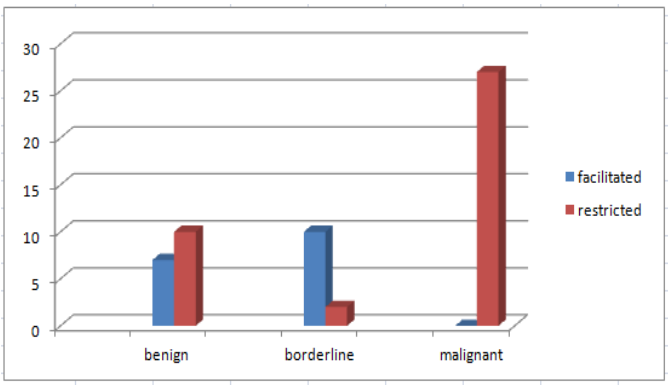
	Sensitivity	**Specificity**	**PPV**	**NPV**	**Accuracy**
Conventional MRI-Radiology	74%	47%	76 %	44%	66%

Table 3:ROIs were placed within the solid component of the predominantly cystic and mixed solid cystic lesions as well as the solid lesions and ADC values were measured.

	Minimum	**Maximum**	**Mean (±SD)**
Benign lesions	**0.7**	**1.8**	**1.12 ±0.22**
Borderline tumors	**0.4**	**1.2**	**0.83 ± 0.34**
Malignant tumors	**0.3**	**1.1**	**0.64 ± 0.25**

Table 4: Relation between pathology and diffusion.

	Sensitivity	**Specificity**	**PPV**	**NPV**	**Accuracy**
DWI # Pathology	89%	41%	78%	64%	75%



(Chart 1)-: chart illustrates the diffusion signal intensity in the different ovarian lesions.

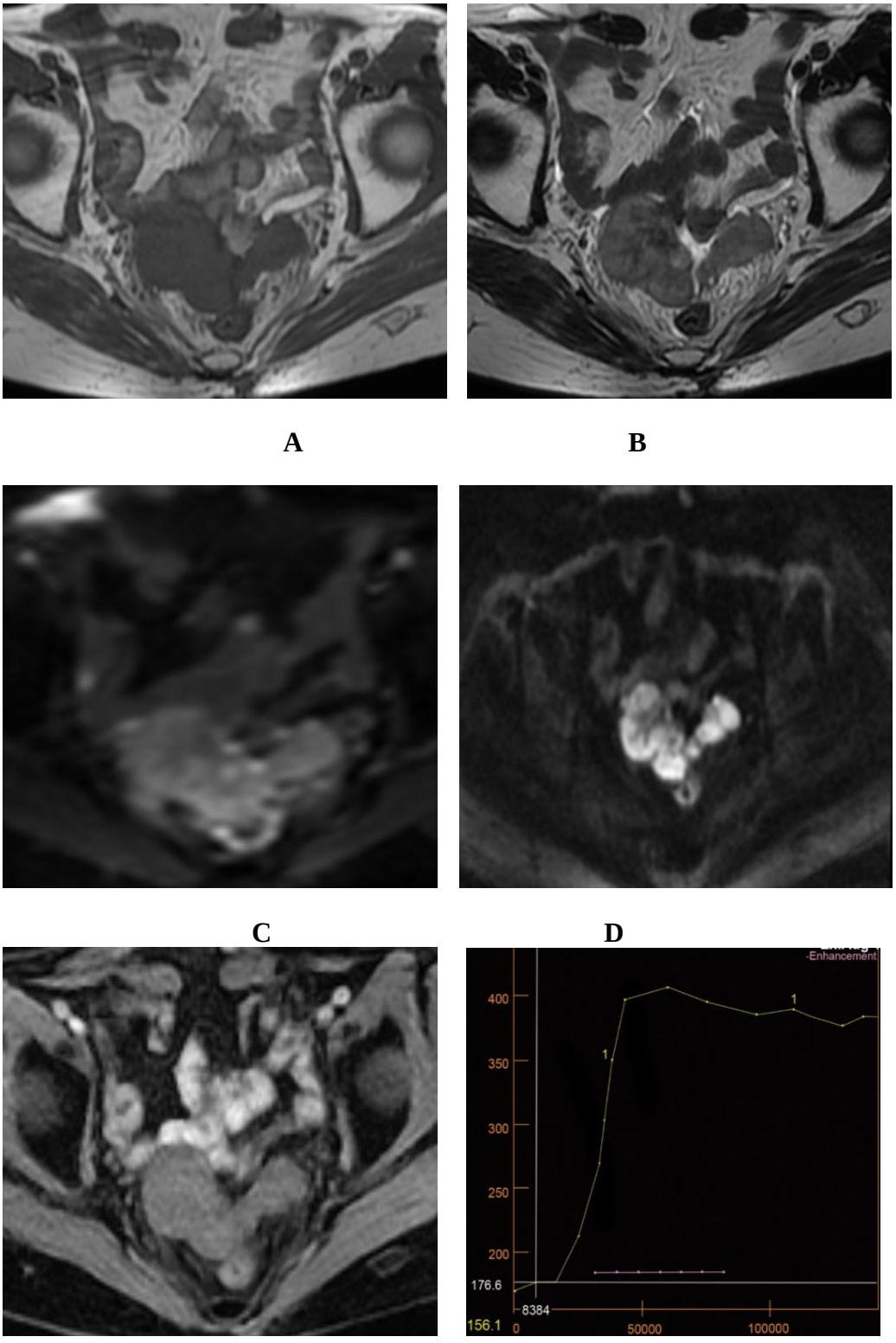
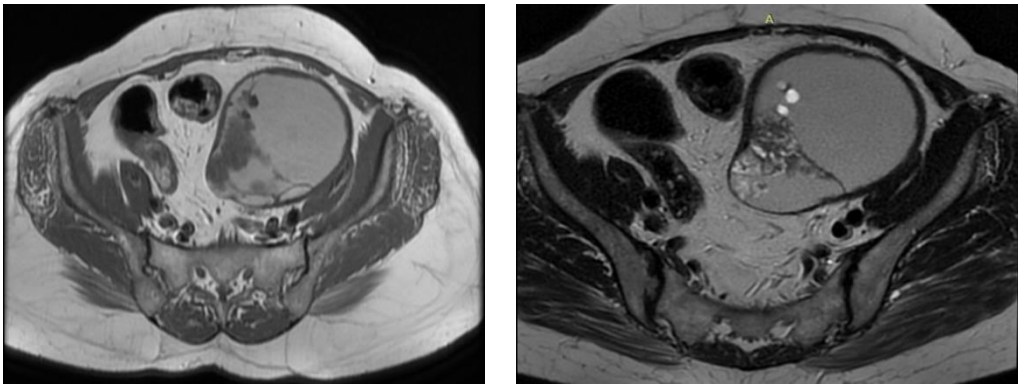
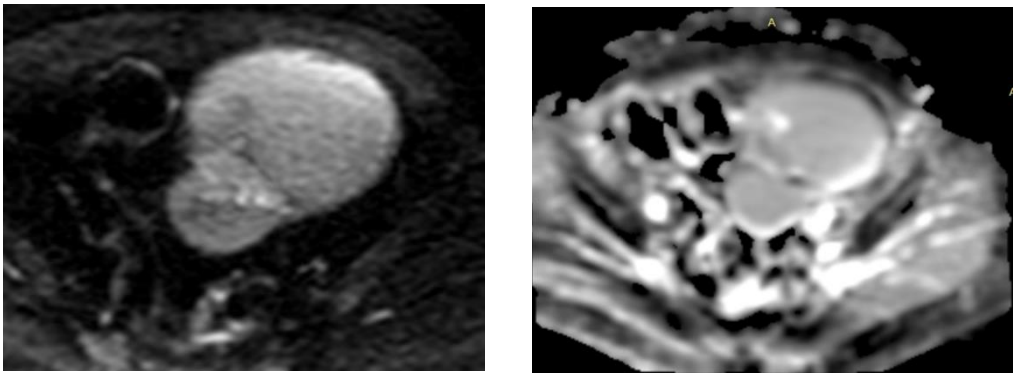


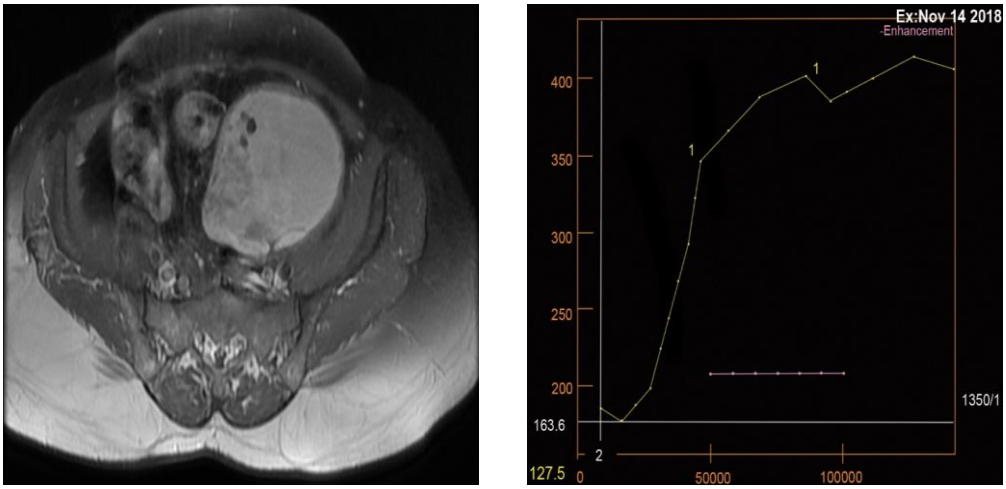
Fig 1: Case (1) 64 year-old female patient with past history of cystectomy for serous cystadenocarcinoma, complaining of abdominal pain. US revealed a bilateral multiple complex adnexal lesions.



A **B**



C **D**



E **F**

Fig 2: Case (2) 56 year-old female patient complaining of abdominal pain with past history of hysterectomy. US revealed a large left complex adnexal lesion.

Discussion

In this study, 70% of the lesions showed restricted diffusion (hyper-intense signal in DWI and hypo-intense in ADC map), whereas 30% displayed facilitated diffusion. All the malignant (n=27, 100%) and two of the borderline lesions (n=2, 16.6%), as well

as 10 (58.8%) benign lesions showed restricted diffusion (3tubo-ovarian abscesses, 1haemorrhagic cyst , 2endometriomas ,2 fibrothecoma ,1 mature cystic teratoma and 1 chronic ectopic pregnancy). We also found that the mean ADC values of the solid components for the benign lesions differed significantly from that of the borderline and invasive malignant lesions ($p \leq 0.001$). Yet there were some overlaps between them in our study.

We concluded that ADC measurement in the solid components was more specific for differentiating benign from malignant lesions. This agrees with LI et. al., who conducted a study, where the mean ADC value of the cystic component did not differ significantly between benign and malignant masses. Mean ADC values of the tumour solid components were also determined for each of the groups, **mean ADC value** for **benign lesions** was 1.69 x 10^{-3} ± 0.25 SD mm^2/s, and for the **malignant** was 1.03 x 10^{-3} ± 0.22 SD mm^2/s. The lower ADC values associated with the malignant group were found to be statistically significant ($p < 0.01$). Their results suggest that an ADC value ≥ 1.25 x 10^{-3} mm^2/s may be an optimal cut off value for differentiating benign and malignant ovarian tumours **(11)**.

In 2012 another study demonstrated that the following factors can be considered predictive of malignancy: the presence of a solid component with high or low signal intensity on T2-weighted images and high signal intensity on DWI with low ADC values (less than 1.20 × 10^{-3} mm2/s) at b = 1,000 s/mm2. On the other hand, the following factors can be considered predictive of a benign mass: the presence of a solid component with high or low signal intensity on T2-weighted images and high signal intensity on DW images with high ADC values (greater than 1.20 × 10^{-3} mm^2/s), or low signal intensity on T2-weighted images and DW images with lower ADC values at b = 1,000 s/mm^2 **(12)**.

In 2008 a study conducted on 123 ovarian lesions, recorded that most malignant ovarian tumours, as well as some of the mature cystic teratomas, showed high signal intensity on **DWI**. Also, they concluded that the **mean ADC value** of the solid portion in malignant tumours did not significantly differ from that in the benign lesions (mean ADC for the benign lesions was 1.47±0.42 and mean ADC for the malignant lesions was 1.41±0.34(x 10^{-3} mm^2/S)). They attributed this finding to the inclusion of sex cord stromal tumours, Brenner's tumour and cyst-adenofibroma; all of which have a dense network of collagen fibres and thus resulting in low ADC values similar to the malignant lesions **(7)**.

In our study, the addition of the DWI improved the sensitivity, PPV, NPV and accuracy of the **conventional MRI** from 74%, 76%, 44% and 66% to 89%, 78%, 64% and 75% respectively. Yet the specificity was decreased from 47 % to 41 %. Such low specificity elicited in our research is explained by the presence of benign cases that have mimicked malignancy on DWI; starting from their misleading signal intensities of restricted diffusion, down to the low ADC values measured such cases include TOA (n=3), Fibrothecoma(n=2), Endometriomas (n=2),Mature cystic Teratoma (n=1)and chronic ectopic pregnancy (n=1) showed restricted diffusion due to predominately solid or mixed cellularity of such lesions .

In 2015 another study found that the solo performance of DWI is not an applicable way to discriminate benign from malignant ovarian masses. DWI can confirm or exclude potential malignancy in suspicious ovarian masses; providing (i) inclusion of the conventional MRI data, (ii) combined analysis of DWI quantitative and qualitative criteria and (iii) awareness of the sequence pitfalls. The sensitivity, specificity, PPV, NPV and accuracy of adding **DWI** to conventional MR imaging was 93.3% , 85 % , 88.5%, 94.4%, and 82.3% respectively compared to 93.3 %, 100 % , 100% ,92.3% , and 95% after adding **DCE-MRI** to the conventional MR respectively **(13)**.

In 2009 a prospective analysis was done to check the possibility of DWI to characterize 77 adnexal masses. They considered the SI at the DWI to be the accurate tool for predicting benign/malignant criteria not the ADC values, in our study ADC value was the most accurate tool **(14)**.

We had 12 **borderline** ovarian tumours which showed variable appearance on DWI. About ten cases showed facilitated diffusion of its solid component with a high ADC value (1.4 $x10^{-3}mm^2/S$) suggesting benign pathology (false negative). Two cases showed restricted diffusion with high signal on DWIs and mean ADC value of 0.8 $x10^{-3}mm^2/S$; suggesting a malignant invasive pathology. Also, borderline pathology is suggested based on its morphological features “presence of vegetation or thick septations”.

Quantitative DCE–MRI provides an accurate method for the prediction of malignancy, particularly in preoperative indeterminate cases **(15)**.

In 2003 another study described that malignant lesions show greater enhancement than benign lesions during the early phase of enhancement rather than the late phase of enhancement. While benign ovarian tumours

showed a gradual increase in enhancement without a well-defined peak, while, borderline ovarian tumours showed moderate initial enhancement followed by a plateau [(16)].

In 2008 another study showed that curve type 3 appeared specific for invasive tumours. Curve type 1 was more frequent in benign than in malignant tumours. No difference was found among the three groups (benign, borderline and malignant) regarding the frequency of curve type 2. However, there was an overlap among the curve types of the benign and borderline lesions; therefore, their capacity to differentiate benign from borderline tumours was low [(17)].

In our work, 7 lesions out of 17 (41.2%) showed steady rise with no definite peak (type 1 curve) while the other ten lesions (58.8 %) showed rapid rise with a plateau, while some of the invasive malignant lesions 18 (66.6 %) showed initial rapid steep early enhancement (type 3 curve). However, there was a great overlap between benign and borderline lesions, as we had 6 borderline tumours (borderline serous cystadenomas) which had type 1 curve. We also had 9 cases of malignant tumours which demonstrated type 2 curve (2 dysgerminoma, 1 mucinous cystadenocarcinoma, 2 granulose cell tumours, 2 serous cystadenocarcinoma and 2 krukenburg).

Conclusion:

DCE and DWIs sequences are good supportive techniques to conventional MRI in the categorization of ovarian masses into benign, borderline and invasive malignant tumours.

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