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Role of diffusion weighted and perfusion weighted imaging in characterization of ovarian tumours

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ABSTRACT

Background: ovarian cancer is the second most common gynecological cancer and the fifth most common cancer in women. Proper management depends on proper preoperative assessment with the help of clinical examination, laboratory tests and different imaging modalities. Radiological evaluation includes ultrasonography (US), computed tomography (CT) and recently magnetic resonance imaging (MRI). Diffusion weighted imaging (DWI) has been established as a useful functional imaging tool in neurologic applications for a number of years, but recent technical advances now allow its use in abdominal and pelvic applications.

Purpose: it was to evaluate the role of diffusion weighted and perfusion weighted MRI imaging in the characterization of ovarian tumours and differentiation between benign and malignant tumours.

Patients and Methods: this study was performed on 24 patients. All patients had US finding of solid or complex adnexal lesions.

Results: DWI & dynamic MRI are significant promising tool factors for characterization of ovarian tumours and differentiation between benign & malignant lesions with high sensitivity, specificity. The sensitivity, specificity and accuracy of detection of the nature of the lesions. Have been increases after adding of DWI & DCE-MRI to the conventional imaging.

Conclusion: Adding of DWI & DCE-MRI to the conventional MRI improves the sensitivity and specificity of diagnosis and allows confident diagnosis and differentiation between benign and malignant lesions.

Keywords: Ovarian tumours, MRI, DWI, ADC, DCE, TTP, MRE, SI max.

Introduction

Ovarian cancer is a leading cause of death among women. It is the second most common gynecological cancer [(1)]. Accurate characterization of an adnexal mass as being benign can avoid unnecessary surgery especially in postmenopausal women and can help young women wishing to preserve child bearing potential to go for conservative surgery [(2)]. MR imaging has shown to be more specific and accurate than US and Doppler assessment in preoperative characterization of complex adnexal masses. In addition, it is the best method in delineation of local spread to the pelvic organs. The signal intensity characteristics of ovarian masses make possible a systematic approach to diagnosis. Mature cystic teratomas, cysts, endometriomas, leiomyomas, fibromas, and other lesions can be accurately diagnosed on the basis of T1- weighted, T2-weighted, and fat-saturated T1-weighted MR imaging findings [(3)].

Diffusion weighted imaging (DWI) and DCE-MRI have recently been shown to be effective in the differentiation of benign from malignant adnexal masses. DWI provides quantitative information about tissue cellularity that may be used to distinguish benign and malignant lesions and distinguish viable tumors from treatment-related changes. DCE-MRI is becoming increasingly important in the evaluation of cancer patient in initial diagnosis and the assessment of response to therapy [(4)].

DCE-MRI of ovarian tumors is recommended for accurate characterization of internal architecture, especially for delineation of necrosis, papillary projections, solid

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components, septations, and peritoneal implants [5].

Aim of the study: it was to evaluate the role of diffusion weighted and perfusion weighted MRI imaging in the characterization of ovarian tumours and differentiation between benign and malignant tumours.

Patients and Methods

Our study was prospective analysis study done on 24 patients referred from Surgery and Gynecology Departments having adnexal lesions based on trans-abdominal/trans-vaginal U/S.

The patients' age ranged from 23 to 65 years with median age 44 years.

The patients' complaints varied between pelvic pain, dysmenorrhea, abdominal pain and abnormal vaginal bleeding. Some presented with more than one symptom.

Pelvic MRI with DWI and DCE-MRI was done for all patients. The examinations was carried at Radiology Department at Ain Shams University Hospitals in the period from August 2016 till February 2018, by Philips Achiva sets 1.5 Tesla (8 channels) using phased array pelvic coil.

- Intravenous administration of 10 mg of an antispasmodic drug was given immediately before MR imaging to reduce bowel peristalsis.

Ethical considerations:
An informed consent was taken from every patient or her guardians about acceptance of participation in the study and knowing the possible risk factors of the given contrast medium. **The study was approved by the Ethics Board of Ain Shams University**.

MR imaging analysis:

MR images were analyzed morphologically as regards:
MR criteria of benign lesions according to [6]:

- High signal intensity on T1WI is considered either fat or blood (e.g. dermoid/teratoma and endomterioma). On fat suppressed images low signal is noted with fat while high signal is still noted in blood.
- Solid masses with very low signal intensity in T2WI are characteristic to fibrous tumor (e.g. ovarian fibroma, or Brenner tumor or pedunculated subserous fibroid).
- Simple cystic tumors with low signal intensity in T1WI and high signal intensity on T2WI with no solid component.

Suggestive MR criteria of malignant lesions according to [6]:
Presence of wall thickness > 3mm, Solid vegetations more than 1cm, Thick septa > 3mm, Areas of necrosis and breaking down, Signs of tumor spread for staging: enlarged lymph nodes, ascites, peritoneal and omental deposit.

Results

This study included 24 female patients with 30 ovarian lesions with ultrasound findings of adnexal lesions.

Statistical analysis:
The tumors were classified pathologically into: 13 benign and 17 malignant tumors.

The age in cases with benign tumors ranged from 23 to 65 years (mean age 35.4 $\pm$ 12.37). While the age in cases with malignant tumors; ranged from 27 to 65 years (mean age 50.8 $\pm$ 11.78).

Benign tumors included (2 serous cystadenomas, 3 endometriomas, 2 mature cystic teratomas, 1 atypically proliferating cystadenoma, 1 fibroma, 2 fibrothecoma, 1 benign granulosa cell tumour, & 1 tubo-ovarian abcess).

Malignant tumors included (6 mucinous cystadenocarcinomas, 3 dysgerminomas, 2 serous cystadenocarcinoma, 1 immature teratoma, 1 clear cell tumour, 2 kruckenberg tumour, 1 granulosa cell carcinoma& 1 endemetrioid adenocarcinoma).

A) According to conventional MRI:
The malignant lesions ranged from 4 to 16 cm with average size 10.45 $\pm$ 3.9 cm while benign

lesions ranged from 4.5 to 13 cm with average size 7.48 ± 2.86 cm.
The diagnosis was based on morphological features, T1, T2 signal intensities.
Fifteen cases showed typical benign morphological criteria whereas fifteen cases showed typical morphological criteria.
Two pathologically proven benign masses were misdiagnosed malignant by the conventional MRI (FP), (one mature cystic teratoma and one benign granulosa cell tumour) and two proven malignant masses were misdiagnosed as benign (FN) (two mucinous cystadenocarcinomas), Table (1).

Table (1): Results of conventional conventional-MRI compared to pathology.

TP	TN	FP	FN	Sensitivity	Specificity	PPV	NPV
17	13	2	2	89.48 %	86.67 %	89.4 %	86.6 %

B) According to DWI:
Twenty cases showed restriction by DWI (high signal in diffusion images & low signal in corresponding ADC map, 17/20 proved to be malignant by pathology (true positive). 3/20 proved to be benign by pathology (false positive): 2 mature teratomas with ADC values 0.8 and 0.7 x 10^{-3} and tubo-ovarian abscess with ADC value 1.1 x 10^{-3}, Table (2).

Table (2): The pathological types according to DWI.

	Frequency	Percentage
Benign	**10**	**33.3 %**
Malignant	**20**	**66.7 %**

Table (3): Results of DWI imaging compared to pathology.

TP	TN	FP	FN	Sensitivity	Specificity	PPV	NPV
17	13	3	0	100 %	81.25 %	85 %	100 %

The different ADC values elicited from the corresponding ADC maps were calculated. ADC values of malignant tumors showed a minimum of 0.4 x 10^{-3} mm^2/s and maximum of 1.1 x 10^{-3} mm^2/s with Mean 0.86 +/- 18 SD, while ADC values of benign masses showed a minimum of 0.6 x 10^{-3} mm^2/s and maximum of 1.8 x10^{-3} mm^2/s with Mean 1.35 +/- 0.41 SD.
In our study, the cutoff value for ADC was 1.1 x 10-3 with sensitivity 100 %, specificity 69.23 %, PPV 81 % and NPV 100 %.

C) According to DCE-MRI:
Fourteen cases showed type I curve (slowly rising enhancement with delayed peak of contrast uptake and delayed washout), 11/14 proved to be benign where 3/14 proved to be malignant.
Eight cases showed type II curve (rapid, steep early enhancement followed by plateau), 1/8 proved to be benign where 7/8 proved to be malignant.
Eight cases showed type III curve (rapid, steep early enhancement followed by rapid washout), 1/18 proved to be benign where 7/8 proved to be malignant.

Table (4): the average values of TTP, MRE, SI max & WIR of benign & malignant lesions.

	Benign	Malignant
TTP	63-125 Average 109.9 +21.25	42-122 Average 67.8 + 24.8
MRE	52-110 Average 70.8+ 15.1	70 -150 Average 115.1 + 19.7

SI max	237 – 1003 Average 456.5 +237.3	480 – 1068 Average 924.2 + 201.9
WIR	2.4 – 16.5 Average 5.5 + 3.8	5 -15.6 Average 12.3 + 3.4

The cutoff value of, TTP, ***MRE***, SI max & WIR was 71 seconds, 77 %, 466% & 9.4 L/s respectively.

Table (5): Results of DCE-MRI compared to pathology.

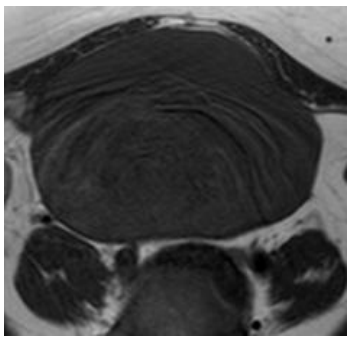
TP	TN	FP	FN	Sensitivity	Specificity	PPV	NPV
17	13	1	1	94.44 %	92.86 %	92.44 %	92.86 %

Our study showed that sensitivity of *DWI* is much higher than conventional MRI and *DCE-MRI* yet; it's much less specific in differentiating benign and malignant lesions, Table (6).

The adding of *DCE-MRI* increased the sensitivity, specificity, PPV and NPV from 89.5 %, 86.7 %, 89.5 % and 86.7 % respectively to 94.4 %, 92.9 %, 94.4 % and 92.9 % respectively.

Table (6): The sensitivity, specificity, PPV & NPV OF Conventional MRI, DWI and the DCE-MRI:

	Conventional MRI	DWI	DCE-MRI
Sensitivity	89.48 %	100 %	94.4 %
Specificity	86.67 %	81.25 %	92.86 %
PPV	89.48 %	85 %	94.4 %
NPV	86.67 %	100 %	92.86 %



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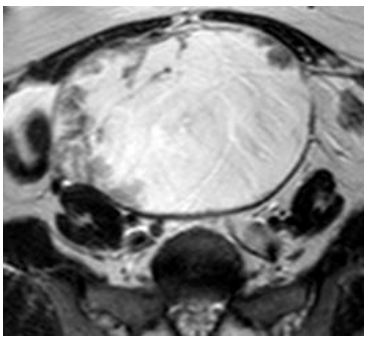

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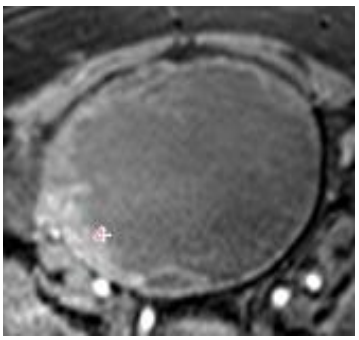

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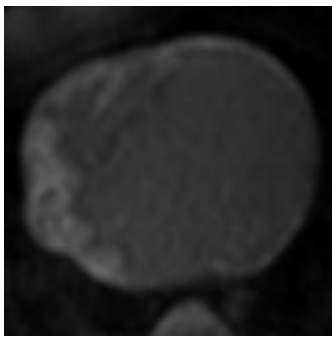

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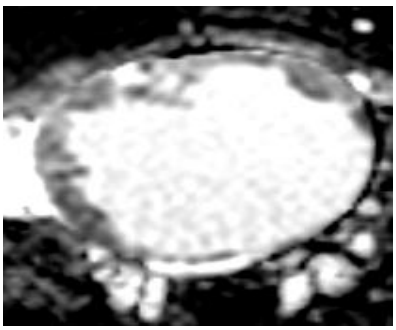

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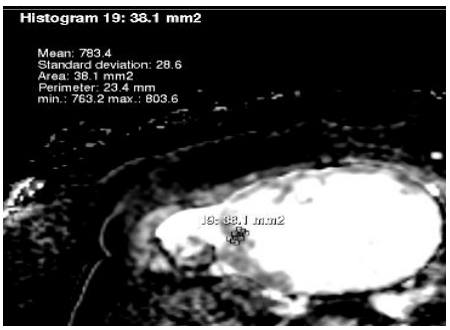

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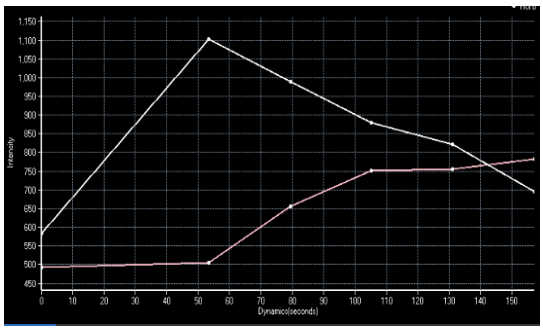

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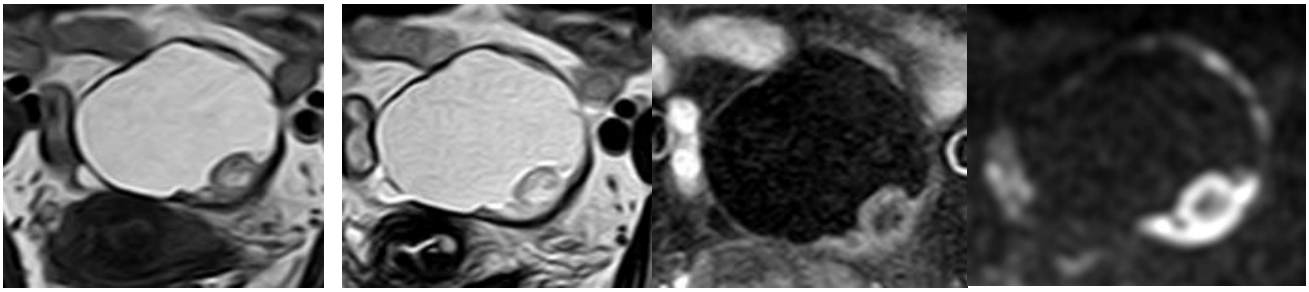
Case (1): 58 years old patient presented with post-menopausal bleeding. U/S revealed large predominantly cystic pelvic mass with mural projections.

(a-c) T1, T2 & Post contrast T1; showed complex cystic right adnexal lesion, displaying low T1WI signal and high T2WI signal with multiple soft tissue nodularities and mural projections, displaying low T1WI & T2WI signal. The lesion shows intense post contrast enhancement of the mural projections and internal septations.

(d-f) DWI, ADC map & ADC value; the mural projections showed high signal on DWI with low signal on the corresponding ADC. ADC value of the solid portion of the tumor was 0.7 x 10^{-3} mm^2/s.

(g) DCE-MRI; the lesion showed rapidly rising curve with early peak of contrast uptake at 79 sec. post contrast injection, SI max. 950%, MRE 120% (higher than myometrial enhancement) with early wash out (Type 3 curve). WIR was 11.4 L/sec & WOR was 2.35 L/sec.

MRI diagnosis according to conventional, DWI and DCE-MRI was malignant ovarian mass. This case was pathologically proven to be papillary serous cystadenocarcinoma**.**



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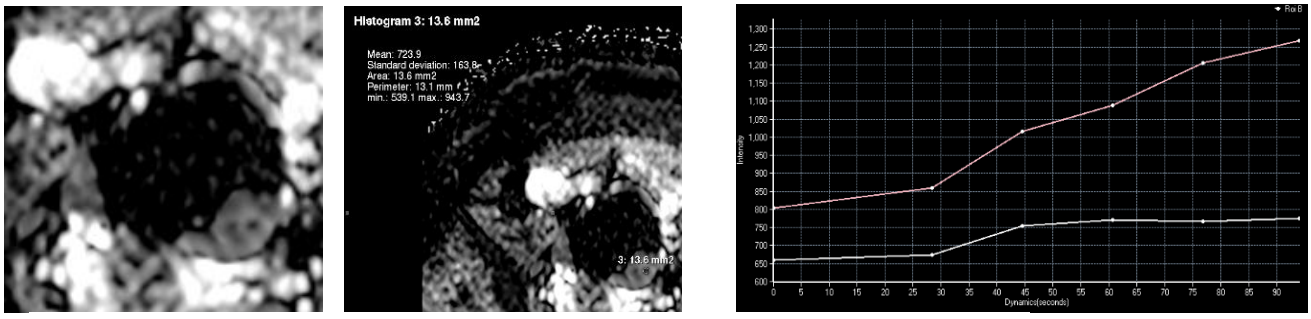

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Case (2): 26 years old patient presented with pelvic pain. U/S revealed complex cystic mass.

(a-c) T, T2 & Post cintrast fat sat images; shows left adnexal complex fat containing cystic lesion with mural nodule. The cystic component of the lesion shows bright signal in T1 & T2WI with suppression in fat sat images. The solid nodule also shows bright T1 & T2 signal with post contrast enhancement.

(d-f) DWI, ADC map & ADC value; the mural nodule shows high signal on DWI with low signal on the corresponding ADC maps. ADC value of the solid portion of the tumor was 0.7 x 10^{-3} mm^2/s.

(g) DCE-MRI; the lesion showed slowly rising curve with delayed peak of initial uptake of contrast at 120 sec. post contrast injection, SI max. 436 %, MRE 52 % (Type 1 curve). WIR =was 3.4 L/sec & WOR = zero.

MRI diagnosis according to conventional, DWI & DCE-MRI benign ovarian mass, likely dermoid although evidence of diffusion restriction and low ADC value. This case was pathologically proven to be mature cystic teratoma.

Discussion

In our study, we evaluated 24 patients with 30 ovarian lesions.

(1) According to conventional -MRI:

Two pathologically proven benign masses were misdiagnosed malignant by the conventional MRI (FP), (one mature cystic teratoma and one benign granulosa cell tumour) and two malignant masses were misdiagnosed as benign (FN) (two mucinous cystadenocarcinomas).

(2) According to DWI:

According to our study, DWI showed 100% sensitivity in its individual performance during the assessment of the included adnexal masses, yet slightly lower specificity (81.25%).

The mean ADC values for malignant lesions were ($0.86 \times 10^{-3} \pm 0.18$ SD mm^2/s), while that for benign lesions were ($1.35 \times 10^{-3} \pm 0.41$ SD mm^2/s) with the p-value = 0.000 (statistically significant if < 0.05)

Such low specificity is explained by the presence of 3 FP cases: Mature cystic teratomas (n=2) with ADC values 0.7×10^{-3} & 0.8×10^{-3} mm^2/s & tubo-ovarian abscess (n=1) with mean ADC value 0.6×10^{-3} mm^2/s. This is attributed to the mixed cellularity of such lesions. The cutoff value of ADC in our study was 1.1×10^{-3} mm^2/s with sensitivity 100 %, specificity 69.2 %, PPV 81 % and NPV 100 %.

A study carried out by Takeuchi ***et al.*** [7] at 2010 on 49 women; all malignant tumors showed high intensity on DWI, whereas only 3 cases of the benign tumors (3 thecomas) showed high intensity. However the presence of low intensity on T2-weighted images was suggestive for benign fibrous tumor. In their study, the ***mean ADC*** value in malignant tumors was 1.03×10^{-3} mm^2/s was significantly lower than that in the benign tumors 1.38×10^{-3} mm^2/s. Using a cutoff ADC value of ***1.15***; malignant lesions had a sensitivity of 74%, specificity of 80%, PPV of 94%, and NPV of 44%. They concluded that low DWI and high ADC intensity may suggest benign lesion, however, it may be occasionally difficult to differentiate benign and malignant lesions only on the basis of DWI. Such suggestion agrees with our study that showed that abundant cellular masses (teratomas & tubo-ovarian abscess) showed high restricted diffusion.

Another study carried out by Koyama T ***et al.*** [8] in 2007 on 35 women 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. Addition of DWI to conventional MRI has increased the specificity from 81% to 85% respectively. In their study the sensitivity of both (MRI and DWI) was 100%.

In contrast in our study, where the specificity decreased from 86.7% to 81.25%. This could be attributed to the three false positive cases in our study (2 mature teratomas and one tubo-ovarian abscess) while in their study they excluded the teratomas and haemorragic cysts. Yet; the sensitivity increased from 89.5% to 100%.

Another study was carried out by **Li *et al***. [9] in 2011 on 127 patients with pelvic masses, (46 benign and 81 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.

In this study; 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 $1.69 \times 10^{-3} \pm 0.25$ SD mm^2/s, and for the *malignant* was $1.03 \times 10^{-3} \pm 0.22$ 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, associated with 90.1 % sensitivity and 89.9 % specificity.

This totally agrees with our study, in which the mean ADC value for malignant lesions was (0.86 x 10^{-3} ± 0.18 SD mm^2/s), while that for benign lesions was (1.35 x 10^{-3} ± 0.41 SD mm^2/s), and cutoff value was 1.1 x 10^{-3} for differentiating benign and malignant ovarian tumors with sensitivity 100 %, specificity 69.2 %, PPV 81 % and NPV 100 %.

Also in their study, the sensitivity, specificity, PPV and NPV of *conventional MR imaging* all have increased from 91.8%, 78.3%, 88.6% and 83.7% respectively to 96.5 %, 89.1%, 94.3%, 93.2%, and 93.1% after adding *DWI* to the conventional MR.

This again agrees to our study where the sensitivity, specificity, PPV and NPV of *conventional MR* increased from 89.5 %, 86.7 %, 89.5 and 86.7 % respectively to 94.4 %, 92.9 %, 94.4 % and 92.9 % respectively after adding *DWI* to conventional MRI.

(3) According to DCE-MRI:

Fourteen cases showed type I curve, eight cases showed type II curve & eight cases showed type III curve.

In our study the sensitivity of MRI was 89.5 % while that of DCE-MRI was 94.4 %. Also the specificity was higher for DCE 92.7 % compared to conventional MRI sequences 86.7 %. So, addition of DCE to the MRI is expected to increase the sensitivity and specificity of examination.

Regarding malignant lesions:

- Time of initial peak of contrast uptake ranged from 42 to 122 seconds with an average 67.7 seconds with cutoff value ≤ 71 indicating malignant lesions.
- MRE% ranged from 70 to 150% with an average of 115.1 % with cutoff value ≥ 77 % indicating malignant lesions.
- SI max ranged from 480 to 1068 with an average 924.2 % with cutoff value ≥ 466 indicating malignant lesions.
- WIR ranged from 5 to 15.6 L/s with an average 12.3 L/s with cutoff value ≥ 9.4 indicating malignant lesions.

On the other side, benign lesions showed:

- Time of peak ranged from 63 to 125 s with an average of 109.9 s.
- MRE% ranged from 52 to 110% with an average of 70.8%.
- SI max ranged from 237 to 1003 with an average 456.5 %.
- WIR ranged from 2.4 to 16.5 L/s with an average 5.5 L/s.

- ***A note is made of WOR ≥ zero (indicating washout) strongly suggests malignant tumours with sensitivity 52.9 %, specificity 92.3 %, PPV 90 % and NPV 60 %.***

A study was done by **Eman *et al.*** [(3)] in 2014 described that there was an overlap between benign and malignant lesions according to the type of curve, as plateau curve was found in 16 masses 11 of them proved to be malignant. Their results showed that malignant lesions had TTP ranged between 30 to 70 s with an average 53 s and MRE ranged from 100% to 180% with an average of 130%. In their study benign lesions, showed TTP range of 70 to 110 s with an average 92 s, and MRE% ranged of 40% to 140% with an average of 73%.

Their results relatively agrees with our results which showed TTP of malignant lesions ranging from 42 to 122 s with an average 67.7 s and MRE ranging from 70 to 150 % with an average 115 %. Also benign lesions showed TTP ranging from 63 to 125 with an average 109.9 s and MRE ranging from 52-110 % with an average 70.7 %.

According to them, MRI sensitivity was 99.9% while that of DCE-MRI was 60%. The specificity was higher for DCE (91%)

compared to conventional MRI sequences (58.3%). In this study; there were 4 false negative cases (3 of them were mucinous cystadenocarcinoma, one was dysgerminoma) and one false positive case (serous cystadenoma).

In our study, there was one false negative case (mucinous cystadenocarcinoma) & one false positive case (tubo-ovarian abscess).

Another study done by **Bernardin *et al.*** [(10)] at *2011*, there was some overlap in the enhancement characteristics between benign and malignant groups using all the semi-quantitative parameters. The smallest overlap was observed using WIR; this provided the most reliable enhancement data for distinguishing between benign and borderline/invasive malignant lesions. They concluded that applying a cut-off WIR $\geq$ 9.5 as predictive of borderline/invasive malignancy and optimal diagnostic performance providing a sensitivity of 67%, specificity of 88%, PPV of 86% and NPV of 71%. This strongly agrees with our study, as using cutoff value of WIR $\geq$ 9.4 for reporting malignant/invasive lesions produces sensitivity of 82.4 %, specificity of 92.3 %m PPV of 93.3 % and NPV of 80 %.

Conclusion

Adding of DWI & DCE-MRI to the conventional MRI improves the sensitivity and specificity of diagnosis and allows confident diagnosis and differentiation between benign and malignant lesions.

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