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Dynamic Contrast-Enhanced Magnetic Resonance Imaging; A Useful Tool for Characterization and Assessment of Ovarian Masses

Rania A Maarof, Ahmed S Abdelrahman, Dhifaf A Habeeb
Department of Radiodiagnosis
Faculty of Medicine – Ain shams University
Corresponding author: Dhifaf A Habeeb; Mobile: 01012411293; Email: Dc.dhifaf@yahoo.com

ABSTRACT

Objectives: To evaluate the diagnostic performance of dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) for the characterization of complex ovarian tumors, by using histologic findings as the reference standard. **Patients and methods:** 25 patients (age range from 24 to 60) with complex ovarian masses underwent DCE-MRI before surgical excision. The study included 8 benign, 3 borderline & 14 malignant masses. The following kinetic parameters were analyzed: enhancement amplitude (EA) in the form of MRE%, time to peak in the form of T max & maximal slope (MS) & correlated with histopathological results.

Results: DCE-MRI achieved higher overall accuracy (85.7%) & specificity (86.5%) than conventional MRI. MRE% was higher for malignant than for benign (p0.001) & borderline masses (p0.002). T max was of shorter duration in malignant than in benign (p, < 0.001) and borderline (p, 0.018) masses. Type III curve was specific for invasive malignant tumors. **Conclusion:** DCE-MRI can be a useful tool in characterization of complex ovarian masses & in differentiating between borderline & invasive malignant neoplasms.

Keywords: Ovarian masses, DCE- MRI, enhancement amplitude, time to peak, maximal slope.

INTRODUCTION

Ovarian cancer is the fifth leading cause of cancer death after bronchial carcinoma, breast, colorectal and pancreatic cancers. Ovarian cancer causes more deaths than any other cancer of female reproductive system; despite accounting for only 3% of all cancers in women. When ovarian cancer is found in its early stages, treatment is most effective [(1).] Adnexal masses are common and challenging diagnostic problem because overlapping imaging features of benign and malignant tumors [(2)]. It is of great importance to characterize an adnexal mass as accurately as possible to guide appropriate management, so treatment options become more specific. This is particularly true for young women who should be offered conservative surgery for fertility preservation [(3)].

US is the first-line imaging investigation for suspected adnexal masses, the disadvantage of ultrasonography (US) includes its limitation for characterization of the masses and staging of malignant masses [(4)]. An adnexal mass is defined as indeterminate on US when it cannot be confidently placed into either the benign or malignant category [(5)]. **C**T is commonly performed in evaluation of a suspected ovarian malignancy, but it exposes patients to radiation[(6)].

CT has a limited role in the primary evaluation and characterization of ovarian lesions; however it can be used in evaluating the extent of the disease, in pretreatment planning including cytoreduction and post treatment follow up[(7)]. MRI can be a valuable problem-solving tool, an adjunctive modality for evaluating adnexal lesions, useful to give surgical planning information without radiation exposure[(6)]**.** More recently developed MRI sequences, like dynamic contrast enhancement sequences provided additional capacities for adnexal lesion tissue characterization[(8)].

Contrast- enhanced MR imaging provides a depiction of the internal architecture of lesions, particularly vegetation in a solid–cystic lesion [(9)]. Dynamic contrast-enhanced MRI (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[(10)].

DCE-MRI can depict the distribution of contrast by measuring variations in vessel and tissue enhancement over time. Variations in contrast enhancement are associated with specific histopathological features of the tumor [(11)] DCE-MRI has increasingly been used in oncology due to the insights it offers into tumor microcirculation. Angiogenesis is a key aspect of the growth and metastasis of malignant tumors, and characterization of microcirculation can therefore be valuable in discriminating malignant from benign tumors[(12)].

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Recent studies evaluated the use of DCE-MR imaging to further characterize adnexal masses. It provides information on tumor vascularity and perfusion. It also provides more post processing quantitative data [13].

DCE- MRI of ovarian tumors is recommended for accurate characterization of internal architecture, especially for delineation of necrosis, papillary projections, solid components, septations, peritoneal implants[14]. And they may help differentiate solid components or papillary projections from clots and debris[15]. DCE-MRI is currently being evaluated as possible predictive and prognostic biomarkers in the context of ovarian malignancy and may play a larger role in routine clinical practice in the future[16].

AIM OF STUDY

To evaluate the utility of dynamic contrast enhanced (DCE-MRI) in the differentiation between malignant, border line, and benign ovarian tumors.

PATIENTS AND METHODS

Type of study

This study is a prospective analysis ethics committee approved by the Faculty of Medicine, Ain shams University, and cases had been supplied by Hospitals of Ain shams university.

- **Study Setting:** Ain Shams University Hospitals: maternity hospital and MRI Unit.
- **Study Population** - The study included women presenting with ovarian masses, who are planned to undergo laparotomy.

Twenty-five patients with ovarian masses underwent DCE-MRI before surgical excision. The study included benign, borderline & malignant masses. The patients were referred from the Obstetrics & Gynecology department to the Radiology department (Women's imaging unit) based on preliminary ultrasound examination used for cases selection.

Inclusion criteria

1. Solid and complex ovarian masses with solid/cystic components.

Exclusion criteria

2. Contraindications to contrast media.
3.Contraindications to magnetic resonance imaging.

Sampling method: The study is a prospective analysis.

Ethical considerations: Ethics committee approved by the Faculty of Medicine, Ain shams University, and cases had been supplied by Hospitals of Ain shams university. **Study tool:**

a-Preliminary US:

b-MR imaging performed on closed MR imaging unit (Achieva, Philips medical system). All patients were imaged by using pelvic phased-array Torso coil. The following kinetic parameters were analyzed:

Statistical analysis

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

RESULTS

Table (1): Comparison between histopathology

Maximal mass dimension by cm	Histopathological Results			ANOVA	p-value
	Benign (N=8)	Borderline (N=3)	Malignant (N=14)		
Mean ± SD	7.43±1.82	10.63±4.38	14.50±4.04	10.417	<0.001**
Range	5.25-A10.25	7-A15.5	6.7-A19.5		

The patients maximal mass dimensions ranged from 5.25-19.5 years old (mean 11.77±4.72 SD.

Table (2): Comparison between histopathological results and results of MRI.

Results of MRI	Histopathological Results			p-value
	Benign (N=8)	Borderline (N=3)	Malignant (N=14)	
Benign	5 (62.5%)	1 (33.3%)	2 (14.3%)	0.046*
Malignant	3 (37.5%)	2 (66.7%)	12 (85.7%)	

This table shows statistically significant difference between histopathological results and results of MRI.

MRE

Table (3): Comparison between histopathological results and MRE%.

MRE%	Histopathological Results			p-value
	Benign	Borderline	Malignant	
MRE%				
Mean ± SD	83.66±25	104.33±36.55	325.46±145.77	<0.001**

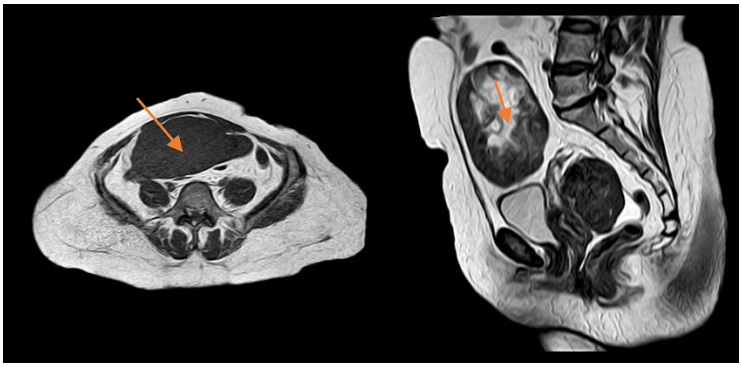
This table shows highly statistically significant difference between histopathological results and MRE%. ***MRE%*** was higher for malignant than for benign masses (p0.001).

T max

Table (20): Comparison between histopathological results and Tmax.

Tmax	Histopathological Results			p-value
	Benign (N=8)	Borderline (N=3)	Malignant (N=14)	
Tmax				
Mean ± SD	201.52±78.88	189.24±103.25	85.21±27.25	<0.001**

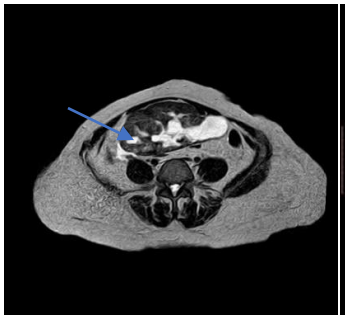
T max was of shorter duration in malignant than in benign (p<0.001) and borderline (p, 0.018) masses.



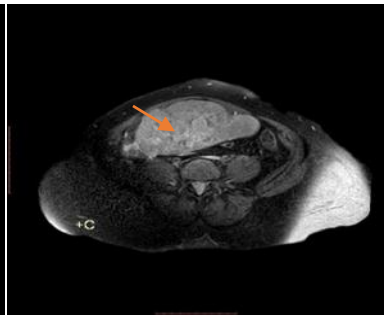
Axail T1W

Saggital T2W

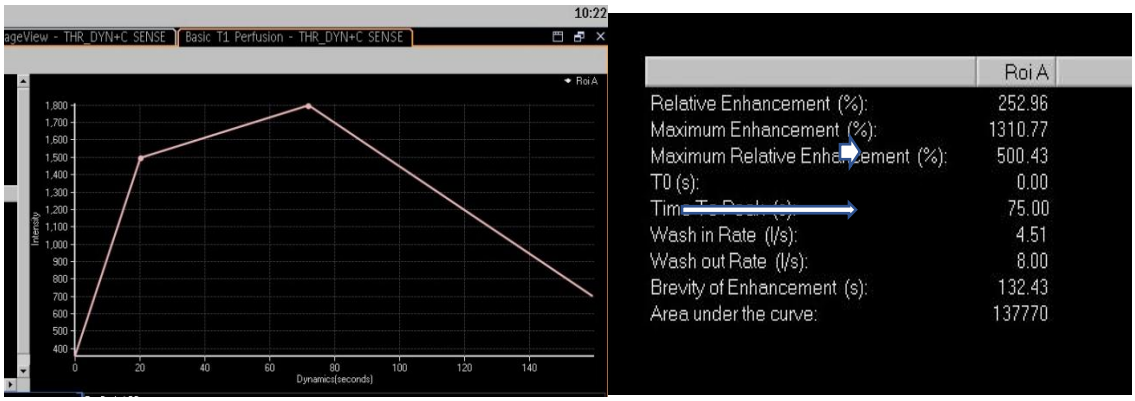
Coronal T2W



Axial T2W



Axial T1W + contrast



DCE-DYNAMIC CURVE

Fig (1):58 years old patient presented with abdominal mass and abdominal pain for few months. US showed large pelvi-abdominal heterogeneous solid mass. ON MRI SHOW:

Bilateral large complex predominantly solid adnexal masses. Both are seen in close relation to the uterus. Both elicit low T1WIs & heterogeneous to high T2WIs signals with intense enhancement in the post contrast images.

DCE-MRI:

The lesion showed early enhancement peak at 75 sec & corresponding MRE% 500.4 & type III early washes out curve pattern

Conventional & DCE MR Diagnosis: Two large adnexal neoplastic masses with suspicious malignant dynamic criteria **Pathology: Malignant Papillary serous cystadenocarcinoma**

DISCUSSION

Angiogenesis is the process of formation of new blood vessels from preexisting blood vessels, which is the fundament of the growth, progression, invasion, and metastasis of nearly all tumors[(17)].Malignant tumors were generally hypervascular with immature and fragile tumor vessels, which could increase the vascular permeability, whereas hypovascularity was characteristic of benign tumors. DCE-MRI could make qualitative, semi-quantitative evaluation of blood perfusion in ovarian tumors based on the different enhancement pattern [(18)].

Analyzing the type of TIC was already widely used in some clinical settings, particularly in differentiating malignant from benign tumors in breast and prostate carcinoma[(19)].

Angiogenesis may differ among different tumor types. Some malignant tumors, such as mucinous adenocarcinoma, may appear to be hypovascular, whereas some benign tumors such as thecoma or sclerosing stromal tumor, show abundant vascularity[(20)].

The EA was higher in malignant than in borderline tumors and higher in borderline tumors than in benign tumors [(21)]

Whereas benign tumors have fewer and relatively mature vessels, which show no obvious change in permeability and microcirculation. Borderline ovarian tumors represented a heterogeneous group of masses with relatively good prognosis and a younger age. A conservative, fertility-sparing surgery could be considered for patients who wish to preserve fertility [(22)]. In this study, blinded analysis of DCE-MRI was done for 25 ovarian masses, the results were compared to the histopathological data.

Dilks & colleagues in 2010[(23)], stated that semiquantitative DCE-MRI provides an accurate method for the prediction of malignancy,

In this study, DCE-MRE had higher specificity, & accuracy (85.7%, 86.5% respectively) than conventional MRI (61.4%, 75% respectively).

Similar results were obtained in Nasr & colleagues study in 2014[(24).] They stated that adding DCE sequence to conventional MRI increases the specificity and the accuracy of examination.

In this work demonstrated that only invasive tumors displayed type III time intensity curve (specificity 100%) similar opinion was stated by

Bernardin & colleagues 2012[(3)] who noted that type III wash out curve is specific for invasive malignant tumors (specificity 100%).

Thomassin-Naggara & colleagues (2008) [(25)] experienced on a population of 37 epithelial ovarian tumors, they demonstrated that only invasive tumors

displayed type III time intensity curve (specificity 100%). Mansour & colleague[26] who plotted that SER curves especially "early washout" pattern is the best parameter to predict the proper diagnosis of ovarian masses so none of the pathological data proved that benign ovarian masses showed Type III curve pattern.

In Li & colleagues 2017 [21] noted that TIC types was accurate for distinguishing malignant from benign ovarian tumors, with a sensitivity, specificity, and accuracy of 83%, 75%, and 82%, respectively.

Another study was carried out by Pegah and colleagues in 2012 [13] on 65 patients with pelvic masses. A plateau curve, was mostly seen with borderline, benign tumors and 11 malignant cases (n=11/22). In 2014 Eid & Abougabal[27] studied the usefulness of subtraction technique in MRI images on population of 40 patients presented with lesions in different parts of the body. They stated that subtraction MRI is very helpful tool in non-vascular MRI applications including the evaluation of the presence of a neoplasm in hemorrhagic masses, complicated cysts.

In 2012 Mohaghegh and Rockall[28] stated that the use of subtraction technique at DCE-MRI enables depiction of true enhancement in ovarian masses within high-signal-intensity lesions.

In this study, MRE ranged from 58 to 142% in benign masses & from 94 to 581% in invasive malignant masses. That is similar to previous studies as Thomassin-Naggara et al., 2008 & Mansour et al., 2015 who confirmed that the MRE was higher for invasive tumors than for benign and borderline tumors, but no significant difference was observed between benign and borderline tumors.

Thomassin-Naggara & colleagues 2008[25], considered the MRE cutoff between benign and malignant tumors (borderline and invasive) about 114% with sensitivity 83% and specificity 72%. While Mansour & colleagues 2015[26], MRE% cut-off was 120%, which is a higher value than other studies they attributed this to the inclusion of few hormone-dependent masses in their study with sensitivity 88% and specificity 71.4%. In 2003, Sohaib and colleagues[29] confirmed that malignant tumors exhibited stronger early enhancement (< 60 seconds) than benign tumors. Thomassin-Naggara& colleagues 2008[25], considered T1⁄2max of 29.7 seconds to be the cutoff value with maximum sensitivity of 92% and specificity of 79%.

In 2014 Nasr & colleagues [24] found that T max cut off value between benign & malignant ovarian tumors was considered 75 seconds.

Mansour & colleagues in 2015[26] considered early T max duration 120 seconds from the start of the dynamic sequence which is longer than other researchers. With specificity, we found out that T max was shorter for malignant than in benign (p,0.001) and borderline masses (p,0.018) but no significant difference was noted between benign & borderline masses. (p, 0.643)

We followed Mansour, et al 2015[26] using the dynamic sequence (3D THRIVE) with large FOV that included the whole pelvis.

Summary and conclusion:

The final diagnosis of an ovarian tumor is based on the histological examination, yet it is desirable to differentiate between benign, border line and invasive ovarian tumors in order to decide if surgery is required, and which type of surgery is appropriate.
Pelvic magnetic resonance (MR) imaging has clearly been demonstrated to be the best imaging technique to characterize complex adnexal masses due to its excellent tissue contrast. Dynamic contrast enhanced MR imaging (DCE-MRI) is a technique which can assess tissue perfusion and tumor neo-angiogenesis by measuring tissue enhancement over time. It also provides more post processing options to aid evaluation of adnexal masses.

Our study used dynamic contrast enhanced MR sequence on 25 patients presented with ovarian masses that had solid components in order to rule out the malignancy in these masses based on their behavior of contrast uptake. DCE-MRI showed higher overall accuracy (85.7%) & specificity (86.5%) than conventional MRI.

CONCLUSION

Our preliminary findings suggest that semi-quantitative DCE-MRI is useful for distinguishing malignant from benign tumors and borderline from benign tumors, but not for differentiating malignant from borderline tumors,
although there is a different TIC type. Therefore, further studies, combining other imaging techniques such as quantitative DCE-MRI, magnetic resonance spectroscopy, and diffusion-weighted imaging, are warranted.

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