The utilization of dynamic contrast-enhanced MRI (DCE-MRI) and Diffusion-Weighted Image (DWI) to characterize indeterminate ovarian masses

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Abstract

Aim: The aim of the present study was to assess the ability of dynamic contrast-enhanced MRI (DCE-MRI) and Diffusion-weighted image (DWI) to describe uncertain ovarian masses.

Methods: The present study was conducted in the Department of Radio-diagnosis and we did transabdominal ultrasound and transvaginal ultrasound for all cases. We investigated 60 patients with 60 adnexal lesions.

Results: The patient's age ranged from 20 to 76 years old (mean 44.46 years). The main complaint was abdominal pain and/or abdominal distension; other cases came with different symptoms as subfertility or irregular vaginal bleeding. The histopathology of the assessed masses were 25 benign, 5 borderline, and 30 malignant. The age range for patients with benign tumors was 20 - 68 years (mean 42 ± 12 years) while those with malignant tumors, their age range was 21- 75 years (mean 45 ± 15.55 years). Benign masses included 8 serous cystadenoma, 7 mucinous cysadenoma, 3 mature cystic teratoma, 3 ovarian fibroma, and 2 fibrothecoma, and 2 tubo-ovarian abscess. There were 5 Borderline tumors (3 serous and 2 mucinous). There were 30 invasive malignant masses (10 Serous cyst-adenocarcinoma, 7 Mucinous cyst-adenocarcinoma, 4 Metastatic krukenburg, 4 Immature teratoma, 3 fibrosarcoma, and 2 clear cell carcinoma). ADC values of malignant tumors showed a minimum of 0.7 × 10−3 mm2/s and a maximum of 1.4 × 10−3 mm2/s.

Conclusion: DCE-MRI and DWI-MRI are noninvasive, readily accessible and without ionising radiation, there are advantages in being able use these techniques to further individualise and benefit patient care.

Keywords: Ovarian, contrast, diffusion, MRI

Introduction

Ovarian cancer is one of the commonest cancers in the world. It is the commonest cause of death in women due to gynecologic malignancy around the world. It has a 5 year survival of 40%.[1] In contrast to other gynecologic cancers, the definitive diagnosis is achieved days after of the index surgery. The diagnosis is by pathology. Preoperative diagnosis based on clinical, laboratory, radiological, and even frozen section is not free of errors.[2] Preoperative biopsy is not offered except when the planed treatment is neoadjuvant chemotherapy or in palliative settings.[3] Ultrasound is the first diagnostic imaging. Conventional Magnetic resonance imaging (MRI) uses T1 & T2 signals. MRI has 76% sensitivity and 97% specificity for diagnosis of uncertain ovarian mass. DCE-MRI has a higher sensitivity and specificity of 81% & 98% (DCE-MRI).[4]

For patients with gynecological malignancies, early, non-invasive and accurate assessment of recurrence is crucial in order to decide whether salvage treatment or palliation is appropriate, thus optimizing not only survival and quality of life, but also resource allocation. It is desirable to identify recurrences before symptoms develop, as survival decreases once patients become symptomatic. Although the majority of recurrences are observed within the pelvis, early detection may be diagnostically challenging. The symptoms can be non-specific, and physical examination of the irradiated pelvis is often limited. For monitoring of patients after treatment for gynecological malignancies, the mainstay is analysis of clinical and biochemical (tumor marker) parameters combined with computed tomography (CT) surveillance. Magnetic resonance imaging (MRI) is usually reserved for problem-solving to clarify the nature of indeterminate lesions, most commonly in the pelvis. Contrast-enhanced MRI, especially dynamic contrast enhanced MRI, has been assessed as a tool for detection of tumor recurrence and distinguishing it from post-surgical and post-radiotherapy changes.[5-7] Recent technical advances in diffusion-weighted imaging (DWI) have greatly enhanced the clinical value of MRI. DWI can provide excellent tissue contrast based on molecular diffusion, and may be able to demonstrate malignant tumors. In combination with conventional MRI, DWI and apparent diffusion coefficient mapping can provide additional information in patients with gynecological malignancies, identifying additional sites of pelvic tumors and improving the degree of confidence in image interpretation.[8-10]

Dynamic enhanced imaging (DCE-MRI) has added to the diagnostic accuracy of these masses, due to its capacity to characterize tumor microcirculation and angiogenesis in malignant tumors.[11,12] It depends on contrast medium leakage from capillaries into the extravascular extracellular space, therefore enabling quantitative analysis with information on the blood flow as well as vascular permeability.[13] It allows proper characterization of internal architecture, delineation of necrotic areas, solid components, papillary projections, septations, and peritoneal implants.[14]

The aim of the present study was to assess the ability of dynamic contrast-enhanced MRI (DCE-MRI) and Diffusion-weighted image (DWI) to describe uncertain ovarian masses.

Materials and Methods

The present study was conducted in the Department of Radio-diagnosis and we did transabdominal ultrasound and transvaginal ultrasound for all cases. We investigated 60 patients with 60 adnexal lesions.

We pursue the International Ovarian Tumor Analysis (IOTA) rules to characterize ovarian mass.[15] MR assessment was done at the magnetic resonance unit. We used 1.5 Tesla machine with body coil as a transmitter and a receiver of radio frequency signals. The MR assessment included T1WI, T2WI, post-contrast fat-suppressed T1WI, and DWI. DWI was done at b0, b500, b1000. Descriptive analysis was done. Data from the MR assessment included the mean size of the cyst or mass, the ADC value, and the morphologic criteria suggesting malignancy. We had executed an individual analysis for conventional MRI, DCE-MRI and DWI concerning their diagnostic performance in the characterization of ovarian masses/cysts. Masses are sent for histopathology after operations.

MRI was performed using a 1.5-T system (n = 60) (1.5T Seimens Magnetom Essenza) using a body coil for excitation and a pelvic phased-array coil for signal reception. The MRI parameters varied throughout the time of MRI data acquisition owing to adaptations of our standard clinical protocol. Peristalsis was suppressed with intramuscular administration of 20 mg of scopolamine butylbromide or 1 mg of glucagon . Axial and sagittal fast-spin-echo T2WIs were acquired with a repetition time (TR)/echo time (TE) of 3300-4800 ms/90-100 ms, a 4-5 mm slice thickness/1 mm gap, a 20- to 24-cm field of view (FOV), and a 192×256-256×256 matrix. Unenhanced T1WIs were acquired in the axial and sagittal planes with a spin-echo TR/TE of 525-700/6-10 ms, a 4-5-mm slice thickness/1 mm gap, a 20- to 24-cm FOV, and a 192×256-256×256 matrix. Axial DWI was obtained along three orthogonal directions using spin-echo-type single-shot echo planar imaging with the following parameters: b value = 0 and 1000 ms/mm2, TR/TE = 3000-4000/60–68 ms, a 3-4 mm slice thickness/no gap, a 24- to 45-cm FOV, and a 102×128-128×192 matrix. In half of the 62 patients (n = 31), after 0.1 mmol/kg gadolinium diethylenetriaminepentaacetic acid (Magnevist; Bayer Pharma) had been administered at a rate of 2.0-3.0 ml/s, followed by a saline flush (15 ml at 2.0-3.0 ml/s), multiphase dynamic images (a 20-seconds acquisition time, 9 sections) were obtained using three dimensional, fast-gradient-echo, T1-weighted fat-suppressed, sagittal or axial sequences (TR/TE = 14-15/7-8 ms, a 2-3 mm slice thickness/no gap, a 28-to 40-cm FOV, and a 128×128-192×256 matrix). Finally, we also obtained delayed (4-5 min later) T1-weighted fatsuppressed axial and sagittal sequences sequentially, with parameters similar to those used before injection of gadolinium diethylenetriaminepentaacetic acid. In the other 31 patients, after a single injection of gadolinium diethylenetriaminepentaacetic acid at a dose of 0.1 mmol/kg body weight, we obtained T1-weighted fat-suppressed axial, sagittal, and coronal sequences sequentially, using parameters similar to those used before injection of gadolinium diethylenetriaminepentaacetic acid.

Statistical analysis

All statistical calculations were done using SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows. Data were statistically described in terms of mean ± standard deviation (± SD) and range, or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using Student t test for independent samples. Chi square (v2) test was performed for comparison of categorical data. Fisher exact test was used instead when the expected frequency was <5. Accuracy was represented using the terms sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy. p values < .05 were considered statistically significant.

Results

Table 1: Patient details

Variables	N%
Complaints	
Abdominal pain	50 (83.34)
Sub fertility or irregular vaginal bleeding	10 (16.66)
Histopathology of assessed masses	
Benign	25
Borderline	5
Malignant	30

The patient's age ranged from 20 to 76 years old (mean 44.46 years). The main complaint was abdominal pain and/or abdominal distension; other cases came with different symptoms as subfertility or irregular vaginal bleeding. The histopathology of the assessed masses were 25 benign, 5 borderline and 30 malignant. The age range for patients with benign tumors was 20-68 years (mean 42 ± 12 years) while those with malignant tumors, their age range was 21-75 years (mean 45 ± 15.55 years).

Table 2: Different ADC values of the included masses

	N	ADC Values
Benign n=25		1.3 - 2 × 10−3 mm2/sec
Serous cystadenoma	8	1.5 - 2 × 10−3 mm2/sec
Mucinous cysadenoma	7	1.2 - 1.5 × 10−3 mm2/sec
Mature cystic teratoma	3	1.3 - 1.5 × 10−3 mm2/sec
Ovarian fibroma	3	1.5 - 1.8 × 10−3 mm2/sec
Fibrothecoma	2	1.2 × 10−3 mm2/sec
Tubo-ovarian abscess	2	1.4 × 10-3 mm2/sec
Borderline n=5		
Serous	3	1.2 - 1.5 × 10−3 mm2/sec
Mucinous	2	1.3 × 10−3 mm2/sec
Malignant n=30		0.8 - 1.2 × 10−3 mm2/sec
Serous cyst-adenocarcinoma	10	0.7 - 1 × 10−3 mm2/sec

Mucinous cyst-adenocarcinoma	7	0.8 × 10−3 mm2/sec
Metastatic krukenburg	4	1.4 × 10−3 mm2/sec
Immature teratoma	4	0.9 × 10−3 mm2/sec
Fibrosarcoma	3	1.2 × 10−3 mm2/sec
Clear cell carcinoma	2	0.9 - 0.9 × 10−3 mm2/sec

Benign masses included 8 serous cystadenoma, 7 mucinous cysadenoma, 3 mature cystic teratoma, 3 ovarian fibroma, and 2 fibrothecoma, and 2 tubo-ovarian abscess. There were 5 Borderline tumors (3 serous and 2 mucinous). There were 30 invasive malignant masses (10 Serous cyst-adenocarcinoma, 7 Mucinous cyst-adenocarcinoma, 4 Metastatic krukenburg, 4 Immature teratoma, 3 fibrosarcoma, and 2 clear cell carcinoma). ADC values of malignant tumors showed a minimum of 0.7 × 10−3 mm2/s and a maximum of 1.4 × 10−3 mm2/s.

Table 3: Analysis of the ovarian lesions size

Dimension	**Benign**	**Borderline**	**Malignant**
Minimum	5.5 cm	6.5 cm	7 cm
Maximum	18 cm	25 cm	28 cm
Mean ± SD	9.1 ± 3.2	13 ± 7.3	12.8 ± 5.03

The malignant and borderline ovarian lesions were bigger than the benign lesions.

Table 4: The performance of the preoperative diagnosis

	Ultrasound	**Conventional MRI**	**DCE-MRI**	**DWI**
TP	22	25	26	28
FN	7	4	3	0
FP	7	6	3	1
TN	12	13	16	17
Sensitivity	75.5 %	88.2 %	92.4 %	100 %
Specificity	67.3 %	74.4 %	88.2 %	94.6 %
PPV	75.4 %	82.8 %	85.5 %	96.4 %
NPV	66.4 %	81.5 %	88.2 %	100 %
Accuracy	82.6 %	81.7 %	90.8 %	96.4 %

The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy for DWI were 100%, 94.6%, 94.6%, 100%, and 96.4% respectively. The performance of DWI was higher than the conventional MRI and DCE-MRI.

Discussion

Ovarian tumors are a group of neoplastic lesions showing a wide and varied spectrum of features according to the specific tumor entity. They can be categorized as benign, low-malignant potential/borderline and malignant subtypes.[4,16,17] The World Health Organization (WHO) provided classification of the ovarian masses based on their histogenetic principles, hence categorizing them with regard to their derivation from

coelomic surface epithelial cells (75% of all ovarian neoplasms), germ cells (15-20%), and mesenchyme (the stroma and the sex cord; 5-10%). Metastatic lesions usually arising from breast, colon, endometrium, gastric and cervical cancers, constitute 5% of ovarian neoplasms.[18]

DWI allows excellent delineation of malignant tumors because of the generally suppressed background noise. However, we consider it necessary to refer to other imaging sequences for sufficient identification of lesion boundaries. We found that the combination of DWI and conventional non-enhanced MRI identified additional sites of pelvic tumors and improved the degree of confidence for image interpretation. Additional advantages of DWI include its completely non-invasive nature and cost effectiveness. DWI does not involve radiation exposure, or oral or intravenous administration of contrast material, and is not uncomfortable for the patient. DWI can be easily added to MR study protocols and no additional time for injection of contrast material is required. In patients with gynecological malignancies, DWI can play an important role in the detection of localized tumor recurrence within the pelvis as well as disseminated peritoneal recurrence. The patient's age ranged from 20 to 76 years old (mean 44.46 years). The main complaint was abdominal pain and/or abdominal distension; other cases came with different symptoms as subfertility or irregular vaginal bleeding. The histopathology of the assessed masses were 25 benign, 5 borderline, and 30 malignant. The age range for patients with benign tumors was 20 - 68 years (mean 42 ± 12 years) while those with malignant tumors, their age range was 21- 75 years (mean 45 ± 15.55 years). The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy for DWI were 100%, 94.6%, 94.6%, 100%, and 96.4% respectively. The performance of DWI was higher than the conventional MRI and DCE-MRI. Dilks *et al*. stated that quantitative DCE-MRI is accurate for malignancy prediction, especially in the setting of indeterminate ovarian masses.[19] Similar results were obtained in Nasr et al. study[20] where adding DCE to conventional MRI imaging augmented both accuracy and specificity.

Kinkel et al[6] found that dynamic contrast-enhanced MRI with analysis of signal intensity-time curves improved the ability of MRI to detect tumor recurrence following radiotherapy in 15 confirmed cases of recurrent uterine cervical cancer. They compared dynamic contrast-enhanced MRI with standard T2WI, and found that the specificity and accuracy increased from 22% and 68% to 67% and 83%, respectively. The peritoneal cavity is a common site for metastatic spread of gynecological malignancies, especially in patients with ovarian cancer. In such patients, MRI is very useful for follow-up of the treatment response and for detection of recurrent disease. It is important to realize that second-look surgery is no longer routine, and that imaging diagnosis of recurrence may obviate a second-look laparotomy, since secondary cytoreduction is only justified if resection is considered likely to leave no residual tumor. dynamic contrast-enhanced MRI is comparable (sensitivity 90%, specificity 88%, and accuracy 89%) to laparotomy (sensitivity 88%, specificity 100%, accuracy 89%) but superior to serum CA-125 analysis (sensitivity 65%, specificity 88%, and accuracy 67%) for detection of residual or recurrent peritoneal and serosal implants in women who have been treated for ovarian cancer.[21] DWI can also clearly discriminate

the abnormal signal intensity of peritoneal dissemination from signals arising from surrounding organs such as the bowel. In our series, the ability of DWI to detect intrapelvic peritoneal dissemination was comparable to that of contrast-enhanced imaging. Fujii et al[22] also showed that DWI using 1.5 Tesla scanner was highly sensitive (90%) and specific (95.5%) for evaluation of peritoneal dissemination in the initial staging of ovarian cancer (n = 26).

Conclusion

DCE-MRI and DW-MRI are important MR imaging techniques which enable the radiologist to move from morphological to functional assessment of diseases of the female pelvis. Table 3 summarizes the added value of DWI and DCE-MRI in evaluation of gynaecological malignancies. However, the reader must be aware that well-designed studies are required to compare the added value of DCE-MRI and DW-MRI to the conventional MRI in staging of gynaecological malignancies and evaluation of tumour response to treatment. DCE-MRI and DWI-MRI are noninvasive, readily accessible and without ionising radiation, there are advantages in being able use these techniques to further individualise and benefit patient care.

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