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ORIGINAL ARTICLE

Role of Magnetic Resonance Imaging in Diagnosis of Endometrial and Cervical Malignancies

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ABSTRACT

Background: Endometrial and cervical cancers are common worldwide for gynecological cancers. MRI has been shown to be the most accurate non-invasive technique for endometrial and cervical cancer staging, which is necessary to make the right medical treatment decision, since accurate staging is crucial for the appropriate treatment. Functional MRI (dynamic contrast, diffusion-weighted imaging) in perfect combination with conventional MRI are used to make correct diagnosis and accurate staging.

Objective: The aim of the study is to assess the role of magnetic resonance imaging (MRI) in staging of endometrial and cervical cancer.

Methods: This study was carried out at Radio diagnosis Department, Zagazig University Hospitals, the present study was carried on 37 patients of endometrial and cervical cancer. Conventional MRI, contrast enhanced MRI and diffusion weighted imaging were done.

Results: The combination of conventional and functional MR images is particularly beneficial for the evaluation of endometrial and cervical carcinoma stages. This study included 37 female patients with postmenopausal bleeding, vaginal abnormal bleeding, vaginal abnormal discharge and pelvic pain due to several pathologies, 24 cases of endometrial carcinoma and 13 cases of cervical cancer. All patients underwent conventional MRI, MRI with contrast and diffusion weighted imaging. Biopsies were made for all cases for tissue characterization and histological types identification.

Conclusion: Our results show that magnetic resonance imaging is the best technique for initial endometrial and cervical tumor staging. In order to obtain high diagnostic accuracy, adequate patient preparation, protocol optimization and MRI reporting expertise are essential.

Keywords: MRI, CEMRI, DWI, Endometrial cancer, Cancer cervix.

INTRODUCTION

The most common female reproductive tract cancer is endometrial carcinoma. The average diagnostic age is 61 years. The rising incidence discovered in recent times is expected to be due both to higher life expectancy and increasing obesity rates. Cervical carcinoma is the third most common malignant in gynecology. The average start-up age is 48 years. The widespread use of Papanicolaou screening and successful in situ carcinoma treatment has resulted in a large decrease in cervical cancer in developed countries [(1)].

Ninety percent of endometrial cancer patients suffer from abnormal vaginal bleeding, most commonly postmenopausal, and bleeding tends to happen early in the course of cancer [(2)].

The main risk factor for cancer cervix is human papilloma virus (HPV), especially subtypes 16 (mainly SCC-related) and 18

(mainly adenocarcinoma-related). Low socioeconomic background, early sex life, multiple partners, immune suppression and smoking are other predisposing factors [(3)].

The International Federation of Gynecology and Obstetrics (FIGO) staging system is the most broadly trained endometrial and cervical cancer staging system. In June 2009, a new update of the FIGO staging system was done, due to modification in our information about the tumor biology. The endometrial and cervical cancer staging system of FIGO explains its different clinical management techniques. Endometrial carcinoma management is mainly surgical, while cervical carcinoma totally depends on the FIGO stage. MR imaging has an essential role in assessing and managing the degree of the disease [(4)].

Adequate pre-operative evaluation of the invasiveness of endometrial carcinoma is essential for surgical planning. Magnetic resonance imaging (MRI) is actually the best method for preoperatively assessing the local invasiveness of uterine cancers [(5)].

MRI is used mainly to assess tumor morphology and local extent; it adequately assesses tumor characteristics with significant prognostic value such as size, endocervical extension, parametrial invasion and pelvic side wall or nearby organs (bladder, rectum) invasion [(6)].

The gynecological protocol for pelvic MR imaging contains axial, sagittal and coronal T2-weighted images. Abdomen and pelvis axial spin-echo T1-or T2-weighted images to describe lymphadenopathy, hydronephrosis and abnormalities of the bone marrow [(7)].

Many studies have noted the additional benefit of dynamic contrast enhancement in the assessment of myometrial invasion in endometrial carcinoma patients [(8)].

Dynamic contrast enhanced T1-weighted gradient echo imaging can improve the description and demarcation of small cervical lesions of 3 mm or more with a sensitivity of 98% and provide helpful information for surgical planning [(9)].

Diffusion-weighted imaging (DWI) plays an extremely approved role in routine cervical and endometrial carcinoma staging as it rises the conspicuity of tumors and helps in image characterization [(8)].

Compared to nearby tissues, the tumor usually shows restricted diffusion, this is seen as a high signal intensity area on diffusion-weighted images and a hypo intensity area on apparent diffusion coefficient (ADC) maps. In general, DWI can adequately illustrate the depth of myometrial invasion of endometrial cancer patients [(8)].

PATIENTS & METHODS

Patients

From May 2018 to December 2018, 37 female patients with endometrial and cervical carcinoma [24 endometrial carcinoma and 13 cancer cervix with ages range from 31 years- to 80 years with mean age group ± SD (57 ± 11.6)] were referred from Obstetrics and Gynecology department to Radio-diagnosis department; Zagazig University Hospitals, after obtaining institutional board review from our hospital. Written informed consent was obtained from all participants and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

All patients were subjected to the following:

1. Full clinical history: Personal history (name, age, sexual activity, past history of gynecological disease, family history of gynecological malignancy). Present history: course of the disease, duration, menstrual history, parity.
2. Clinical examination: patients assessed by PV examination, Speculum examination, Palpation (under anesthesia).
3. MRI examination: Carried out using: (1.5 Tesla) super conducting MR imager

(Philips Achieva) using a standard pelvic coil. The patient was in a supine position throughout the examination with head first.

Technique

Positioning

Patients were positioned in supine position and were instructed not to move during the examination. Surface coil was placed over the pelvis.

Pelvic MRI protocol

a. Localizer images in Axial, coronal and Sagittal planes.
b. Fast spin echo T1-weighted echo (FSE) (TR 500 ms, TE 10 ms, matrix 320 ×512, slice-thickness: 3-4mm with an interslice gap of 1–2 mm, FOV 240mm and a flip angle of 90) in axial oblique, coronal and sagittal plane.
c. Fast spin echo T2-weighted images (FSE) (TR 3000 ms, TE 100 ms, matrix 256×512, slice-thickness: 3-4mm with an interslice gap of 1–2 mm, FOV 240mm a flip angle of 90) in axial oblique and sagittal plane.
d. MR imaging with contrast:

All the patients were subjected to intra-venous Gadolinium Diethylene Triamine Penta Acetic acid (GD-DPTA) with dose 0.1-0.2 mmol /kg BW. Post contrast axial oblique and sagittal T1 spin echo with fat suppression was performed utilizing the following parameters TR 600 ms, TE 14 ms, matrix 205×512, slice-thickness: 3-4mm with an interslice gap of 1–2 mm, FOV 240mm and a flip angle of 90).

Most commonly, dynamic contrast-enhanced T1-weighted fat-suppressed images are acquired at time of 30, 60, and 120 seconds after administration of contrast material, Next, delayed phase at time of 3–4 minutes after administration of contrast material in axial oblique T1-weighted fat-suppressed along the axis of the uterus.

In endometrial cancer, the dynamic contrast improves the accuracy as it improved tumor-to-myometrial contrast that is generally seen on delayed (2–4 minutes after administration of contrast material) images, with most endometrial tumors appearing hypointense against the enhancing myometrium. An additional benefit of contrast-enhanced imaging is that small tumors that may be difficult to define at T2-weighted imaging may appear hyper vascular in the early arterial phase.

In cervical cancer, the dynamic contrast improves the accuracy as it depicts small cervical tumors. It also depicts bladder wall involvement in those with advanced disease.

The Dynamic curve in malignant tissue demonstrate rapid, intense enhancement followed by a relatively rapid washout compared to normal tissue.

e. Diffusion weighted magnetic resonance imaging:

Carried out on the same MR imager using a Single-Shot Spin-Echo type echo planar sequence under free breathing with the following parameters (Time of repetition “TR” 2900 ms, Echo time “TE” 70 ms, matrix 512×512, slice-thickness 4mm with an interslice gap of 1-2 mm and FOV 240 mm) were acquired on the axial plane.

The diffusion-sensitizing gradients were done with a b factor of 0-500 and 1000 s/mm^2 for each patient. ADC maps were automatically reconstructed for all diffusion weighted images and used for the measurement of ADC value.

Image interpretation:

Cases were revised and analyzed to assess:

-Signal intensity and homogeneity (homogenous or heterogeneous) on T1 and T2 weighted images compared with that of adjacent myometrium.

-Tumor morphology (tumor size, characteristics, also assessment of enhancement pattern on post contrast image).

-Detection of the junctional zone on T2-weighted images as a band of low signal intensity just beside the endometrium, myometrial invasion was detected when it is disrupted by lesions.

-Vaginal wall invasion (disruption of low-signal intensity vaginal wall).

-Parametrial invasion (disruption of low-intensity cervical stromal rim).
-Pelvic sidewall invasion (extension of tumor within 2 mm of pelvic sidewall, hydroureter and hydronephrosis).
-Bladder/bowel mucosal involvement (tumor infiltrating bladder/bowel mucosa).
-DW-MR images were observed in combination with conventional MRI for anatomical correlation of the lesion.
-ADC examination the largest possible region of interest (ROI) was put on the lesion on a single image slice. Care was taken to avoid contamination of this ROI by adjacent normal tissue or by areas of fluid/necrosis by referring to conventional T2-weighted image. The mean ADC value is measured to every lesion.

STATISTICAL ANALYSIS

The findings of imaging studies were evaluated and correlated to clinical and histopathological results. Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy intervals were calculated.

RESULTS

This study included 37 female patients, they were "24" cases of endometrial carcinoma and "13" cases of cancer cervix. Regarding age distribution in endometrial carcinoma patients, their ages ranged from (40 to 80 years) with the mean age was 61 years; the most common age group was 60-70 years old. Regarding age distribution in cancer cervix patients, their ages ranged from (30 to 70 years) with the mean age was 50 years; the most common age group was 50-60 years old. Regarding the pathological types, the most common pathological type of endometrial carcinoma in our study was endometrial adenocarcinoma seen in 11 patients which represents (45.7%) of the total, the most common pathological type of cancer cervix in our study was cervical squamous cell carcinoma seen in 8 patients which represents (61.5%) of the total, as demonstrated in table (1). Many clinical symptoms were shown in our study, the commonest presentation was postmenopausal bleeding which represents 62.5% in patients with endometrial carcinoma and 46.2% in patients with carcinoma of the cervix. Other symptoms were offensive watery discharge and abnormal vaginal bleeding which represents 12.5% and 25% respectively in patients with endometrial carcinoma and 30.8% and 23% respectively in patients with carcinoma of the cervix as shown in table (2). Our study shows that most malignant endometrial lesions show low signal intensity on T1WI and heterogeneous signal intensity on T2WI with heterogeneous contrast enhancement. And the most malignant cervical lesions show iso signal intensity on T1WI and relatively high signal intensity on T2WI with intermediate contrast enhancement as shown in table (3). The mean ADC values among the studied group of endometrial and cervical carcinoma as shown in table (4). The staging of 24 cases of endometrial cancer in our study was as shown in table (5). The staging of 13 cases of cervical cancer in our study was as shown in table (6). In our study, the overall accuracy of the MRI in staging of endometrial and cervical malignancy is 91.6% and 92.3% respectively. According to sensitivity, specificity, PPV and NPV of combined role of conventional and functional MRI in endometrial and cervical cancer staging as shown in table (7).

Table (1): Pathological types among 37 patients with endometrial and cervical cancer

Endometrial		
Pathology	Number	Percentage %
-Endometrial adenocarcinoma	11	45.7
-Endometrioid carcinoma	4	16.7
-Papillary serous carcinoma	4	16.7
-Clear cell carcinoma	1	4.2
-Adenosquamous carcinoma	1	4.2
-Endometrial sarcoma	3	12.5
Total	24	100
Cervical		
Pathology	Number	Percentage %
-Cervical squamous cell carcinoma	8	61.5
-Adenocarcinoma of cervix	3	23.1
-Cervical leiomyosarcoma	2	15.4
Total	13	100

Table (2): Clinical symptoms among 37 patients within the study

Symptoms	Endometrial		Cervical	
	Number of patients	Percentage %	Number of patients	Percentage %
-Post-menopausal bleeding	15	62.5	6	46.2
-Offensive watery discharge	3	12.5	4	30.8
-Abnormal vaginal bleeding	6	25	3	23

Table (3): The MRI signal intensity of endometrial carcinoma and cancer cervix

Lesion	**No of patient**	**T1WI**	**T2WI**	**Post contrast**	**Diffusion**
Endometrial carcinoma	-24	-Low SI	-Heterogenous (15) -High SI (9)	-Intermediate enhancement (10) -Heterogenous enhancement (14)	-Restricted
Cervical carcinoma	-13	-Iso SI	-High SI (9) -Iso SI (4)	-Intermediate enhancement	-Restricted

Table (4): The mean ADC values among the studied group of endometrial and cervical carcinoma

Endometrial carcinoma	
Mean ± SD	Range
0.77 ± 0.097 x10-3mm2/s	0.621 – 0.931 x10-3mm2/s
Cervical carcinoma	
Mean ± SD	Range
0.69 ± 0.195 x10-3mm2/s	0.201 – 0.964 x10-3mm2/s

Table (5): Staging of endometrial carcinoma

MRI Stages	**Intact JZ**	**Myometrium invasion**			**Cervix invasion**	**LN**	**Parametrium**	**Bladder or rectum**
		No infiltration	Sup infiltration	Deep infiltration				
Stage I (N=18)	0	0	10 (1A)	8	0	0	0	0
Stage II (N=2)	0	0	1	1	2	0	0	0
Stage III (N=3)	1	1	1	1	2	3	0	0
Stage IV (N=1)	0	0	1	0	0	0	1	1

Table (6): Staging of endometrial carcinoma

MRI Stages	Growth pattern	Extension	LN	Parametrium invasion	Bladder or rectum			
	Anterior wall	Posterior wall	Combined	Intrauterine	Extrauterine			
Stage I (N=3)	1	1	1	0	0	0	0	0
Stage II (N=7)	1	3	3	6	0	3	5	0
Stage III (N=2)	1	0	1	0	0	2	2	0
Stage IV (N=1)	0	0	1	1	1	1	1	1

Table (7): The sensitivity, specificity, PPV and NPV of combination of conventional and functional MRI in detection of endometrial and cervical tumor staging

Endometrial carcinoma				
Stage	Sensitivity	Specificity	PPV	NPV
IA (less than 50% myometrial invasion)	100 %	100 %	100 %	100 %
IB (more than 50% myometrial invasion)	87.5%	100%	100%	94%
II (cervical stroma invasion)	100%	100%	100%	100%
IIIC (Metastases to the pelvic or paraaortic lymph nodes)	66.7%	100%	100%	95.5%
IV (Invasion of bladder or bowel mucosa or distant metastases present)	100%	100%	100%	100%
Cervical carcinoma				
Stage	Sensitivity	Specificity	PPV	NPV
IB1(limited to the cervix)	100 %	100 %	100 %	100 %
IB2 (limited to the cervix)	100 %	100%	100%	100 %
IIA (upper 2/3 of vagina)	66.7 %	100 %	100 %	91 %
IIB (parametrium invasion)	100 %	100 %	100 %	100 %
IIIA (lower 1/3 vagina)	100 %	100%	100%	100 %
IIIB (pelvic side wall)	100 %	100 %	100 %	100 %
IV (Spread to adjacent organs or distant organs)	100%	100 %	100 %	100%

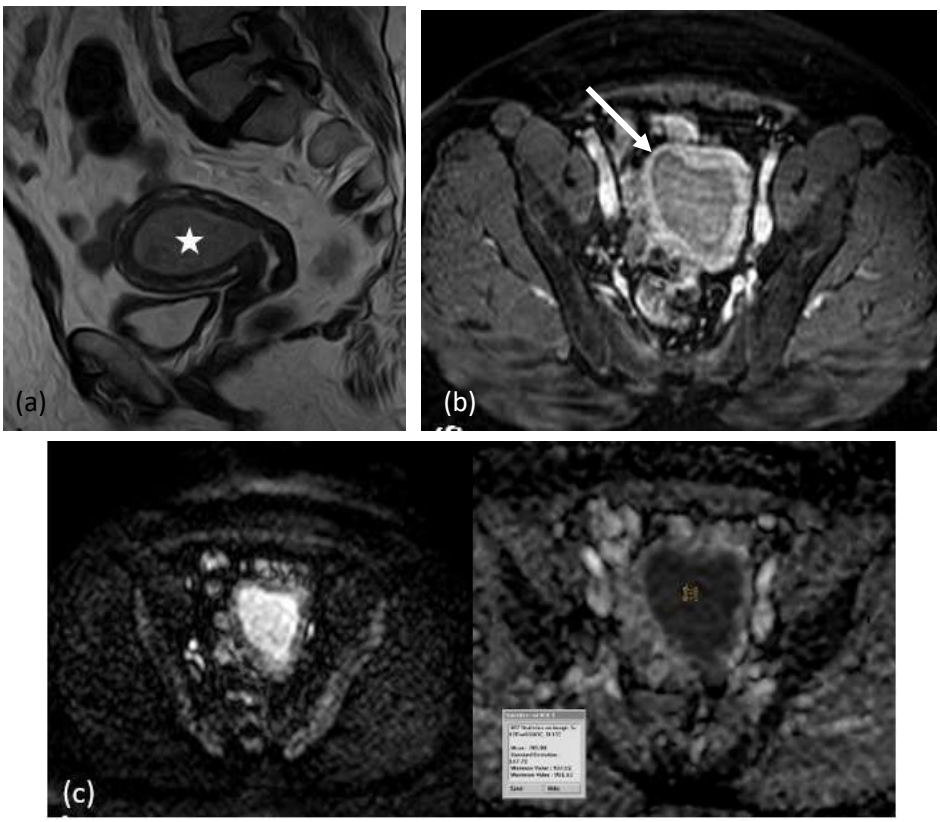

Figure 1. Endometrial adenocarcinoma, (stage IB):
As the endometrial mass invades more than 50% of the thickness of the right anterior myometrium that was proved by histopathology
(A) Sagittal T2-weighted Fast Spin Echo: shows soft tissue expanding mass (star) displaying intermediate signal intensity reaching the lower uterine segment.
(B) Axial T1WI post contrast Fat suppression: shows intense enhancement of the mass. The mass invading the right anterior aspect of the myometrium up to the outer third (white arrow).
(C) Axial DW image and ADC map: show endometrial mass with high signal intensity in DW image and low signal intensity in ADC map, denoting restricted diffusion with ADC value $0.785x10^{-3}$mm/s.

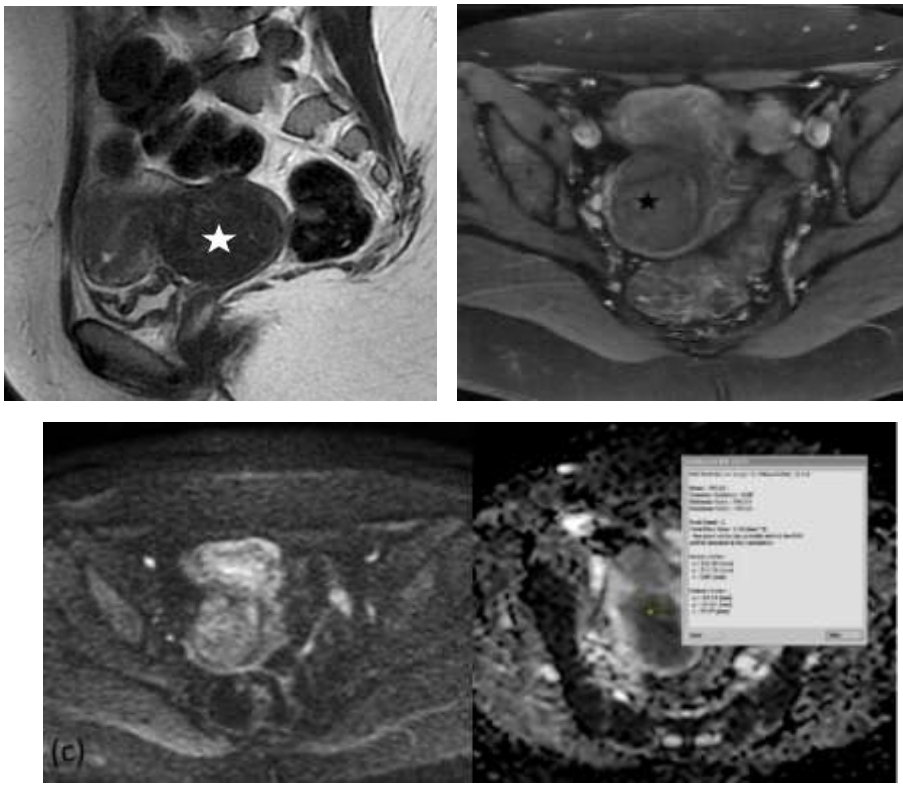

Figure 2. Cervical squamous cell carcinoma, (stage IB2, Clinically visible lesion >4.0 cm in greatest dimension**):**

(A) Sagittal T2-weighted Fast Spin Echo: shows large well-defined soft tissue intensity mass at the cervix region bulging anteriorly (star), displays intermediate to high T2 signal intensity with poor line of cleavage with the low signal cervical stroma.

(B) Axial T1WI post contrast Fat suppression: shows minimal enhancement of the mass (star) with early enhancement.

(C) Axial DW image and ADC map: show cervical mass with high signal intensity in DW image and low signal intensity in the ADC map, denoting restricted diffusion with ADC value $0.745x10^{-3}$mm/s.

DISCUSSION

Endometrial cancer patients are mainly treated with hysterectomy; therefore, staging is performed during surgery and histological analysis. Magnetic resonance imaging (MR) can adequately describe the extent of endometrial cancer during diagnosis and help stratify the risk, which dictates the therapeutic course, in combination with the tumor grade and histologic subtype [(10)].

During clinical examination, cervical carcinoma is staged because many tumors cannot be operated during patient presentation. Principles of preoperative MR imaging are not formally involved in the revised FIGO staging system, as cervical carcinoma is more common in developing countries, with minimal imaging resources. However, MR imaging is highly sensitive and specific for illustrating essential prognostic factors and is also recommended as a clinical examination assistant when available [(7)].

The combination of conventional and functional MR images is particularly helpful in evaluating essential prognostic factors such as tumor size, parametrial and pelvic side wall invasion, nearby organ invasion and lymph node metastases [(11)].

This study included 37 female patients; they were 24 cases of endometrial carcinoma

and 13 cases of cancer cervix. All the patients underwent Conventional MRI, MRI with contrast and diffusion weighted imaging. Biopsies were performed for all cases for tissue characterization and to identify the histological types.

In our study we found that the most common age group in endometrial carcinoma is an average of (40-80) years and that the mean age of the studied group was 60.75 ± 9.78. Similar figure was observed in the study conducted by *Habib et al* [12] that the age of the patients ranged from (40-78) years and the mean age was 53.4 ± 7.29.

We also found that the most common age group affected by cancer cervix was between (30-70) years old and that the mean age of the studied group was 50 ±10.56. Similar figure was observed in the *Mansour et al* [13] study, which reported that the age of the patients ranged from (30-80) years old and the mean age was 49.

The commonest symptom presented by Habib et al [12] in endometrial carcinoma was post-menopausal bleeding with a total percentage (75%) similar figure is noted in our study as the most common presenting symptom was postmenopausal bleeding with a total percentage 62.5% of the cases.

The commonest symptom presented by Dhoot et al [14] in cancer cervix was irregular uterine bleeding with a total percentage (86.6%) while the commonest symptom presented in the current study was postmenopausal bleeding with a total percentage 46.2%.

In our study, endometrial adenocarcinoma represents (45.7%) of cases, indicates the commonest histological type of endometrial malignancy. This incidence was almost compatible with studies conducted by Kierans et al [15] and Habib et al [13], which showed that the most common pathological type of endometrial malignancy examined was endometrial adenocarcinoma, which accounted for 94% and 90% respectively of the total cases studied.

In our study, squamous cell carcinoma represents (61.5%) of cases indicates the commonest histological type of cancer cervix. This incidence was nearly compatible by the studies done by *Mansour et al* [13] and *Article et al* [16], which reported that the most common pathological type of the examined cancer cervix was the squamous cell carcinoma representing 72% and 90.7% of the total studies cases respectively.

Endometrial cancer in our study was recognized as a heterogeneous to hyperintense mass in T2WI, hypointense in T1WI and displayed intermediate or heterogeneous contrast enhancement in accordance with Haldorsen et al [17] that endometrial cancers appear as hyperintense masses in T2-weighted, isointense in T1WI and show intermediate enhancement images irrespective to histopathological type.

Cervical cancer was identified in our study as a mass of intermediate to hyperintense on T2WI, isointense on T1WI and show intermediate enhancement keeping with *Shweel et al* [18] reported that cervical cancers appear as hyperintense masses on T2-weighted, isointense on T1WI and show intermediate enhancement images regardless of histopathologic type.

Rauch et al [1] concluded that all endometrial and cervical cancers appeared hyperintense on DW images. The malignant tissue ADC value was significantly low in comparison to the normal tissue; as the mean ADC values ($\times 10^{-3}$ mm^2/s) were as follow: Endometrial Carcinoma 0.86 and Cervical Carcinoma 0.75. These corresponded to our study which suggests that all endometrial and cervical malignant tissue appeared to be hyperintense on DWI and the ADC value measurement was significantly low; as the mean ADC values ($\times 10^{-3}$ mm^2/s) were as follows: Endometrial Carcinoma 0.77 and Cervical Carcinoma 0.69.

In agreement with study conducted by Hameeduddin et al [19], MRI can better determine the size, location and extension of endometrial and cervical tumors to nearby tissues as it has high soft tissue definition and multiplanar scanning capacities in comparison to the FIGO clinical stage results.

In our study, the overall accuracy of the MRI in endometrial and cervical malignancy staging is 91.6% and 92.3% respectively. Keeping with the study by Rauch et al [1] shows 89% sensitivity with 99% specificity.

CONCLUSION

In our series, we evaluated the role of the conventional and functional MRI in endometrial and cervical cancer diagnosis and staging.

MRI in our opinion is the optimal imaging modality in terms of accuracy for assessment of tumors, and plays an essential role in staging for proper therapeutic planning. To achieve high diagnostic accuracy, we need a good patient preparation, protocol optimization and MRI reporting skill.

Our results indicate that MRI is the proper noninvasive modality for endometrial and cervical tumors detection and staging, and least time-consuming technique, that play an essential role in treatment decision.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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