Research Article

The Role of Dynamic Post Contrast Enhanced and Diffusion Weighted Magnetic Resonance Imaging in Detection of Endometrial Carcinoma

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Abstract

This study to assess the role of dynamic MRI and MRI diffusion functional imaging modality in assessment of endometrial carcinoma using T2WI and contrast enhanced T1 MRI images. **Patients and methods:** The study carried out in women imaging unit at Radiology department, Minia University hospital. It will be conducted on 40 female patients with suspicious uterine lesion. Initially based on ultra-sound findings. **Results:** Our study was performed on 40 patients, their age ranged from 42 to 65 years and their mean age was 52.4 years. Regarding marietal state, Endometrial carcinoma is suspected more in married women about 30 patients from our study (75%). **Conclusion:** Our study supports the value of Dynamic post contrast enhanced MRI for evaluation of an abnormal endometrium in conjunction with MRI DWI. Specifically, abnormal signal of an endometrial abnormality on DWI, as well as irregularity of the endo-myometrial interface or of a focal endometrial lesion, were the most helpful MRI features in assessment of endometrial lesions.

Keywords: dynamic MRI, contrast enhanced T1 MRI images.

Introduction

Endometrial carcinoma is the leading malignant tumor of the female genital tract in industrialized countries. Over the last decade the annual incidence has remained stable with an estimated 25.1 cases per 100. 000 women.(1)

The vast majority of endometrial cancer is diagnosed at an early stage with atypical uterine bleeding in postmenopausal age. The 5-year overall survival is 81.7%, but it varies broadly from 20 to 91 % for different tumor histologies and stages.(2,3)

For radiologists it is important to incorporate the histopathological subtypes I or II in their reporting. These subtypes differ not only with regard to histology and risk factors, but also in clinical features, including stage at presentation, risk of dissemination and in recurrence rate, type I accounts for 80–85 % of endometrial cancers, it is estrogen-responsive and has a favorable prognosis.(4)

Histologically it constitutes endometrioid adenocarcinomas grade I and II. Endometrial cancer type II is characterized by rapid tumor progression and a biological behavior often similar to ovarian cancer. Histologically it comprises endometroid cancer grade 3, and other rare histologies, e.g. serous cancers, clear cell cancers and carcinosarcoma/mixed Müllerian tumors.(4)

Surgical staging with total abdominal hysterectomy and bilateral salpingo-oophorectomy has been the mainstay of therapy in endometrial cancer. Findings at staging also guide subsequent adjuvant treatment. There is ongoing controversy on the value of routine pelvic and para-aortic lymphadenectomy in early endometrial cancer surgery.(4)

Recently a trend towards tailored lympha-denectomy is seen in many cancer centers, as it has been shown that only patients with intermediate or high-risk endometrial cancer benefit from pelvic and paraaortic lymphadenectomy.(4,5)

Internationally, the practice of preoperative MRI evaluation of patients with endometrial

cancer differs widely. According to the American College of Radiology (ACR) appropriateness criteria "MRI should be the preferred imaging modality for treatment planning, when available", as it allows best overall assessment of the disease.[6]

The National Comprehensive Cancer Network (NCCN) guidelines advise MRI when cervical invasion is suspected but also in pre-treatment evaluation of type II endometrial cancer.[7]

The European Society of Urogenital Radiology guidelines recommend MRI in high and intermediate risk cancers, in suspected advanced disease and before lymph node sampling.[8]

In 2015 a multidisciplinary European expert consensus meeting on endometrial cancer advised MR imaging in apparent stage I endometrial cancer to assess the depth of myometrial invasion, when tailored lymph node dissection is performed. However, alternatively, expert ultrasound (US) and/or intraoperative pathological exams are other options.[4]

Patients can be divided into three risk categories based upon histopathological tumour increasing evidence that when findings of staging MRI and hysteroscopic biopsy are combined, women at high risk of lymph node metastases can be identified preoperatively.[9,10]

MRI findings also contribute in triaging and guiding neoadjuvant therapy in advanced endometrial cancer in multidisciplinary consensus conferences.[4,11]

Evaluation of abnormalities of the endometrial cavity poses a significant diagnostic challenge for radiologists and gynecologists.[12]

This challenge reflects a combination of the wide range of appearances and potentially overlapping imaging features of the normal endometrium, influenced by patient's menopausal status and phase of menarche, and of a large spectrum of benign and malignant endometrial pathologies, including endometrial hyperplasia, sub-mucosal fibroid, endometrial polyp, and endometrial cancer.[13]

In addition, such suspicion for endometrial pathology may be based on clinical grounds due to abnormal vaginal bleeding, or based on an abnormal appearance of the endometrium as an incidental finding on radiologic imaging performed for other indications. While endometrial biopsy and curettage serve as the mainstay for diagnosis, these procedures are invasive and not without complications, cause patient discomfort, cannot be performed or are non-diagnostic in 2–28% of attempts[14,15], and often yield inaccurate diagnoses due to sampling error.[16,17]

Thus, reliable non-invasive methods are required to assist in formation of a preoperative diagnosis and appropriate triage of patients for more invasive testing such as endometrial biopsy and D&C. Given its low cost, ease of use, and proven accuracy, transvaginal ultrasonography is generally considered the primary imaging modality for initial evaluation of suspected endometrial pathology.[18]

However, key sonographic findings of endometrial thickening and heterogeneity, as well as of the presence of a focal endometrial lesion, are non-specific and overlap between the previously noted benign and malignant disorders.[19,20]

Alternatively, magnetic resonance imaging (MRI) may also play a key role in the evaluation of suspected endometrial pathology.[18,21,22]

Indeed, a number of studies have identified a variety of MRI features related to endometrial morphology, signal intensity, and enhancement characteristic as useful for distinguishing between benign and malignant endometrial pathology.[13,23,24]

Nonetheless, findings have been variable, if not conflicting, between studies[22]; overlap between benign and malignant cases continues to be reported[22]; and the role of conventional MRI in evaluation of suspected

endometrial pathology remains unclear.[25]

More recently, diffusion weighted imaging (DWI) has been applied for characterization of endometrial lesions. For instance, a number of studies have demonstrated restricted diffusion in endometrial carcinoma than in other benign endometrial lesions. However, the actual clinical role of DWI in evaluating suspected endometrial pathology remains uncertain from such studies. As these studies evaluated DWI findings in isolation, the relative performance of DWI and conventional MRI findings with respect to one another in evaluation of endometrial pathology was not assessed in these studies. More important, whether DWI provides additive value to conventional MRI is unknown. Therefore, the purpose of the current investigation is to evaluate the utility of both conventional MRI and DWI in differentiation of benign from malignant endometrial abnormalities[22, 26, 27]

Aim of the study

To evaluate the specificity of dynamic contrast enhanced MRI and MRI diffusion in diagnosis of endometrial carcinoma in patients with abnormal uterine bleeding.

Patient and method

Prospective study had been carried out at Minia university hospital at period from October 2018 till June 2020 on 40 patients were included in the study after given written informed consent.

- **Inclusion criteria:-**
  1- Patient's age ranging from 40 to 60 years of age.
  2- patients with symptoms including abnormal vaginal bleeding, abdominal pain, and vaginal discharge, and their gynecological and ultra-sonographic (transvaginal and/or abdominal).
  3- Abnormal endometrial thickening was observed in ultrasound (transvaginal and/or abdominal) examination.
  - Endometrial thickening was defined as an increase of the endometrial thickness over 5mmin post- menopausal women and increased thickness of endometrium non-compatible with the expected thickness in proliferative or secretory phases in reproductive women (decided by a clinician according to clinical and sonographic findings)
  4- Patients with MRI features of endometrial carcinoma.
- **Exclusion criteria:-**
  1- Patients with extra uterine bleeding source.
  2- Patients with contra indication to endo-venous contrast injection (e.g chronic renal insufficiency).
3- Bilateral hip prosthesis
4- No surgical procedure post MRI.

MRI technique

All patients underwent pelvic MRI on either a 1.5 T [MAGNETOM Avanto (n = 22), Symphony (n = 13), or Sonata (n = 7]), Siemens Healthcare, Erlangen, Germany)]
The patient lying supine on the table, with the arms along her body, by means of a 16-channel phased- array body coil. The patient was asked to fast 6 h before the examination and to void 1 h before it; moreover, 20 mg of buty lscopolamine bro-mide (Buscopan) were administered intramuscularly just before the examination beginning to further reduce bowel motion.

MRI pulse sequences and image parameters.[28]

High-resolution T2-W images (T2-WI) and CE T1-Weighted images (CE T1-WI) were acquired along three orthogonal planes(para-sagittal, para-axial and para-coronal), according to endometrial cavity longest axis, whereas DW images (DWI) were acquired on two planes only (para-axial and para-sagittal). Para-sagittal images were acquired using a feet-to-head phase encoding, with 100% phase oversampling, in order to minimize motion arti-facts, whereas para-axial and para-coronal images were acquired using a latero-lateral phase encoding with a phase oversampling as large as required by patient's dimensions. B-values of 0, 500, 800and 1000 s/mm2were used for DWI; apparent diffusion coefficient (ADC) maps were generated from isotropic diffusion-weighted images using a software. CE T1-WI were acquired after an intravenous bolus injection of 0.1 mmol/kg of gadobutrol (Gadovist, Bayer, Berlin, Germany), followed by a 20 ml saline flush, starting 60 s

after contrast material injection. (Fig 31)

Using a torso phased-array coil. Acquisition parameters of the included sequence varied somewhat between cases given the long time period of the study, as well as use of different scanners and imaging planes and slight adjustment of parameters by the technologists based on patient size.

Multiplanar turbo-spin echo T2-weighted imaging (T2WI) angled to the plane gap; field of view (FOV) 250–275 mm with 80–100% rectangular FOV; matrix 512×200–210; 2 signal averages; receiver band width 195–200 Hz/voxel, parallel imaging factor 2], axial in and-opposed-phase gradient-echo T1-weighted imaging (T1WI) [TR 150–240; TE 2.0–2.2/5.0–5.3 at 1.5 T.

Flip angle (FA) 80◦; slice thickness 6–8 mm; 20% section gap; FOV 350–360 mm with 80% rectangular FOV; matrix 256×180–220; 1 signal average; receiver bandwidth 380–930 Hz/voxel; parallel imaging factor 2], and dynamic 3D fat-suppressed spoiled gradient echo T1WI (TR/TE 3.2–4.2/1.2–2.0 ms; FA 10–15◦; slice thickness 1.4–3.0 mm; 20% section gap; FOV 220–275 mm with 100% rectangular FOV; matrix 256×130–146; 1 signal average; receiver bandwidth 490–530 Hz/voxel; parallel imaging factor 2) performed before and at multiple time points following intravenous administration of 0.1 mmol/kg of gadopentetate dimeglumine (Magnevist, Bayer HealthCare).

All examinations also included a fat-suppressed single-shot echo-planar DWI sequence of the pelvis performed using tridirectional motion-probing gradients and b-values of 0, 50, and 500 s/mm2 (n = 13) or 0, 500, and 1000 s/mm2 (n = 39), with inline reconstruction of the apparent diffusion coefficient (ADC) map and the following parameters: TR/TE 2100–2500/76–82 ms; slice thickness 6–8 mm; FOV 350 mm with 75–80% rectangular FOV; matrix 144×192; 3 signal averages; receiver bandwidth 1300 Hz/voxel. DWI was performed in the sagittal plane in cases ordered for suspected endometrial or other uterine pathology. (Table2)

- The specimens for pathologic evaluation were obtained by endometrial biopsy or D&C

- All patients were examined for the presence or absence of each of the following MRI features:

- Focal endometrial lesion regardless of contour
- Focal endometrial lesion with irregular margins
- Irregular endo-myometrial interface on T2WI.
- Irregular endo-myometrial interface on post-contrast T1WI.
- Endometrial heterogeneity on T2WI.
- Decreased T2 signal of the endometrial abnormality.
- Increased T1 signal of the endometrial abnormality relative to normal endometrium.
- Increased enhancement of the endometrial abnormality on early post-contrast T1WI.
- Increased enhancement of the endometrial abnormality on late post-contrast T1WI.
- Increased signal of the endometrial abnormality on DWI when compared to the normal visualized endometrium using the highest obtained b-value, and decreased signal of the endometrial abnormality on the ADC map when compared to the normal visualized endometrium.
- Increased DWI and decreased ADC signal was determined as compared to normal outer myometrium.
- The maximal endometrial thickness on sagittal T2-weighted images as well as the maximal diameter of the focal endometrial abnormality in any plane in cases scored as positive for presence of a focal endometrial lesion.

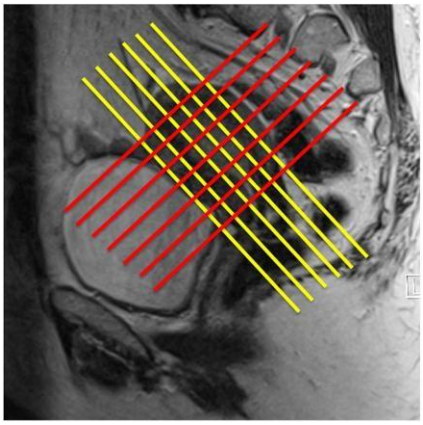

Fig. 1. MRI scanning plans. Sagittal Turbo Spin Echo (TSE) T2-eighted image (TR/TE3200/82 ms) showing the correct scanning plans: para-axial (red lines) and para-coronal (yellow lines) images should be acquired orthogonal to the endometrial cavity.[28]

Results

Table (1): Demographic and clinical data of the studied patients (N=40)

Variable	NO	%
Age		
Range	42-65	
Mean ±SD	52.4±6.7	
Marital status		
Married	30	75%
Unmarried	10	25%
BMI		
Range	20-35	
Mean ±SD	28.7±4.2	
Normal weigh	10	25%
Over weight	10	25%
Obese	20	50%
Bleeding		
Yes	35	87.5%
No	5	12.5%
Pain		
Yes	10	25%
No	30	25%
Associated with Fibroid		
Yes	5	12.5%
No	35	87.5%

Our study was performed on 40 patients , their age ranged from 42 to 65 years and their mean age was 52.4 years.

Regarding marital state, Endometrial carcinoma is suspected more in married women about 30 patients from our study (75%)

Regarding patients body mass index, Endometrial carcinoma was suspected more evident in obese patients Their BMI ranged from 20 to 35 and Mean BMI was 28.7
Regarding the clinical presentation of endometrial carcinoma , Abnormal vaginal bleeding was the common symptom in bout 87.5% while pain is least common symptom.
The endometrial carcinoma may be associated with other pathologies as fibroid (found in 12.5%).

Table (2): histopathology of the studied patients (N=40)

Variable	NO	%
Positive	38	95%
Negative	2	5%

Histopathology was done to all 40 patients, 95% (38 patients) were confirmed endometrial carcinoma.

Table (3): MRI finding of the studied patients (N=40)

Variable	NO	%
T2WI		
Hyper intense	22	55%
Non homogènes hyper intense	18	45%
T1post Contrast		
Negative	2	5%
Positive	38	95%
Diffusion		
Positive	40	100%
ADC		
High	8	20%
Low	32	80%
Depth of endometrial invasion		
Less than 50%	33	82.5%
More than 50%	5	12.5%
No	2	5%

Different MRI sequences in diagnosis of 40 patients suspected as endometrial carcinoma, Most of cases, the endometrial abnormalities attain hyperintense signal at T2WI (55%) while non-homogenous hyperintense signal characteristics in (45%)
At T1 WI post contrast study, the endometrial abnormality shows delayed enhancement than the adjacent myometrium in most cases (95%) while no enhancement of the abnormality detected in (5%)

At DWI sequences, all cases showed hyperintense signal (positive) with corresponding low ADC in 80 % (true restriction of signal) and high ADC in 20% (Non true restriction).

The depth of myometrial invasion is accurately measured in T2WI and post contrast T1WI, We found that there was 5% no myometrial invasion, less than 50% myometrial invasion 82.5% and more than 50% myometrial invasion 12.5%.

Table (4): relation of Demographic and clinical data to histopathology (N=40)

Variable		**Positive N=38**	**Negative N=2**	**P**
Age	Range Mean ±SD	42-65 52.2±6.6	48-64 56±11.3	0.4
Marital status Married (30) Unmarried (10)	 30 10	 28(93.3%) 10(100%)	 2(6.7%) 0	0.4
BMI	Range Mean ±SD	20-35 28.8±4.001	21-35 28±9.8	0.4
Normal weigh(10) Over weight(10) Obese **(19)**	10 10 19	9(90%) 10(100%) 19(95%)	1(10%) 0 1(5%)	0.5
Bleeding **Yes** **No**	 35 5	 33(94.3%) 5(100%)	 2(5.7%) 0	0.5
Pain **Yes** **No**	 10 30	 10(100%) 28(93.3%)	 0 2(6.7%)	0.4
Fibroid Yes No	 5 35	 5(100%) 33(94.3%)	 0 2(5.7%)	0.5

Table (5): MRI finding of the histopathology (N=40)

Variable		**Positive N=38**	**Negative N=2**	**P**
T2WI Hyper intense Non homogènes hyper intense	 22 18	 20(90.9%) 18(100%)	 2(9.1%) 0	0.1
T1post Contrast Negative Positive	 2 38	 0 38(100%)	 2(100%) 0	0.001*
Diffusion Positive	 40	 38(95%)	 2(5%)	0.001*
ADC High Low	 8 32	 8(100%) 30(93.8%)	 0 2(6.2%)	0.4
Depth of endometrial invasion Less than 50% More than 50% No	 33 5 2	 33(100%) 5(10%) 0	 0 0 2(10%)	0.001*

Table (6): Sensitivity, Specificity, PPV, NPV and Accuracy % of T2W1, T1 contrast (N=40)

	Sensitivity	Specificity	PPV	NPV	Accuracy %
T2WI	47.4%	100%	100%	9.1%	50%
T1post Contrast	100%	100%	100%	100%	100%

Discussion

This study was to evaluate the utility of dynamic post contrast enhanced MRI in conjunction with MRI DWI in assessment of endometrial carcinoma MRI features relating to both morphology and signal characteristics in diagnosis of endometrial carcinoma. Malignant endometrial pathologies were significantly more likely to exhibit irregularity of a focal lesion or of the endo-myometrial interface, as well as increased signal on high b-value DWI and decreased ADC. Numerous other qualitative features, including endometrial heterogeneity, presence of a focal endometrial lesion, and T1-, T2-, and post-contrast characteristics of the endometrial abnormality. In addition, measurements of endometrial thickness and of the diameter of focal endometrial lesion. support the role of DWI in characterization of endometrial carcinoma.

Endometrial carcinoma appeared hyperintense onT2-WI, in comparison to the adjacent myometrium, in the majority of the cases, but iso- or hypo-intensity, representing a possible confounding factor for imaging evaluation, On the other hand, in our series EC showed diffusion restriction, appearing hyperintense on DWI and hypointense on ADC maps.

Therefore, DWI and CE T1-WI are more reliable than T2-WI for correctly identifying endometrial carcinoma. If singly considered, both T2-WI and DWI performed better than CE T1-WI in the detection of deep myometrial infiltration by EC. In our series MRI accuracy in recognizing deep myometrial infiltration by EC was not improved by the addition of CE-T1-WI to T2-WI, whereas a discrete accuracy improvement was warranted by the addition of DWI to T2-WI. This increase in accuracy was the direct consequence of an increase in sensitivity not burdened by a loss of specificity , brought by the addition of DWI. However, no statistically significant differences were found in the accuracy of the different MRI sequences and sequences combination in recognizing deep myometrial infiltration.

The highest sensitivity for this aim was warranted by CE T1-WI, whereas the highest specificity byT2-WI. The association of a second imaging sequence to T2-WI, regardless if CE-T1-WI or DWI, increased MRI accuracy in recognizing cervical stromal infiltration by EC The most significant confidence increase was highlighted by the addition ofT2-WI to DW ones and must be interpreted as the direct consequence of getting a highly anatomical template (T2-WI) with which to compare the extremely high tissue contrast resolution but low spatial resolution diffusion-weighted images.

We also note that increased signal on high b-value DWI demonstrated the highest inter-reader agreement of any of the features that showed a significant difference in frequency between benign and malignant endometrial abnormalities.

DWI depends on increased cellularity of endometrial cancer compared with the various benign endometrial pathologies. On our study. the enhancements pattern may vary among different types of endometrial carcinoma Findings on conventional MRI, irregularity of the endo-myometrial interface suggest malignancy.

Although irregularity of the interface was observed in most of malignant cases. The junctional zone undergoes changes in thickness and appearance over the course of the menstrual cycle and can demonstrate an appearance resembling that of the endometrium at certain phases, thus possibly accounting for the apparent irregular endo- myometrial interface identified in a small fraction of benign lesions in our study. In addition, it has been reported

that evaluation of the myometrium in the presence of endometrial lesions on T2WI and post-contrast T1WI may be difficult due to the endometrial lesion exhibiting signal intensity similar to that of the normal myometrium . This latter factor may have contributed to an irregular endo-myometrial interface serving as a significant predictor of endometrial malignancy, independent of DWI findings, indicative of a potential greater level of reader experience required for reliable visual assessment of this particular feature.

The clinical value of our study is in assisting radiologists and clinicians in establishing an appropriate level of suspicion for endometrial malignancy when an abnormal appearance of the endometrium is encountered on MRI, thereby directing further management. It is hoped that the study's findings may allow for a more confident and reliable diagnosis of endometrial carcinoma. of course, MRI findings must still be integrated with clinical features including patient age, menopausal status, history of abnormal bleeding, and use of hormonal therapy or other medications. In addition, the majority of diagnoses were established by endometrial curettage and biopsy, which is prone to sampling error.

Conclusion

While an irregular endo-myometrial interface on post-contrast T1WI was also a significant independent predictor. While requiring confirmation in larger series, these findings may assist radiologists and clinicians in establishing an appropriate level of suspicion for endometrial malignancy when an abnormal appearance of the endometrium is encountered on MRI.

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