Research Article

Evaluation the Role of Mri in Detection of Uterine Causes of Post-Menopausal Bleeding

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Abstracts
Background: Postmenopausal bleeding is quite common and worrisome symptom accounting for ٥٪ of all gynecological outpatient's department attendances. **Objectives:** study the accuracy of MRI in identifying endometrial lesion in comparison to hysteroscopy in cases of postmenopausal bleeding. **Methods:** Before MRI examination, the patients were routinely questioned about any of the conditions which might be a contraindication for MRI examination such as cardiac pace makers, metallic intracranial or thoracic surgical clips and metallic prosthetic implants [especially ferromagnetic hip prosthesis]. **Results:** There were insignificant differences in frequencies of different pathological types between histopathology and MRI
Keywords: MRI, D&C and Hysteroscopy.

Introduction
The role of MRI in gynecologic oncology has evolved during the past two decades. There is now a substantial body of evidence that MRI is useful in evaluating malignant conditions of the pelvis (Hricak et al., ٢٠٠٠). MRI has been shown to be superior to CT in staging of endometrial and cervical carcinoma. In addition, there is evidence that MRI may aid in differentiating radiation fibrosis from recurrent tumor[1]ak et al., ٢٠٠٠). The accuracy of MRI assessment of lymph nodes is similar to that of CT; both rely on size criteria to detect the presence of metastases. However, more recently, lymph node–specific contrast agents have emerged as useful tools for determining the presence of metastases in the lymph nodes[1]. (Hricak et al., ٢٠٠٠).

MRI has been shown to minimize costs in some clinical settings by limiting or eliminating the need for further expensive or more invasive diagnostic or surgical procedures[1]. (Hricak et al., ٢٠٠٠).

A D&C does not sample the entire endometrium and can miss up to ١٠٪ of disease. Due to its associated operative risks, D&C is falling out of favour[2]. (Oehler & Rees, ٢٠٠٤).

Hysteroscopy permits direct visualization of cervical canal and uterine cavity. Diagnostic hysteroscopy is both accurate and feasible in diagnosis of intrauterine abnormalities. As diagnostic hysteroscopy predominantly performed in the outpatient clinic, and therapy in an inpatient setting, an accurate diagnosis is important to direct treatment at the specific pathology and avoid needless surgery. Moreover, it may contribute to prognosis of expected quality of life[3]. (Van Dangen H et al., ٢٠٠٧).

The objectives is to study the accuracy of MRI in identifying endometrial lesion in comparison to hystero-scopy in cases of postmenopausal bleeding

Subjects and Methods
This study had been conducted at El-Minia Maternity and Pediatric University Hospital started at December ٢٠١٠ to January ٢٠١٣. The aim of this work to study the accuracy of MRI in identifying endometrial lesion in comparison to hysteroscopy in cases of postmenopausal bleeding

Sample size calculation
The study consisted of ٤٠ patients, this sample size was calculated by a specific program called

EPI-INFO and for calculation of the sample by this method the following data are needed.

Ethical issue

Following ethical guidelines of the research, an approval was taken from the Department Ethical Committee before the start of research. Also written informed consent was taken from each patient .The objectives of the study and the details of the used procedure were explained for each patient.

Patients Eligible Criteria
Inclusion Criteria:
- Postmenopausal women over ٥٠ years presented by bleeding
- No general cause of abnormal uterine bleeding.
- No history of drug use that can cause vaginal bleeding.
- No history of recent hormonal treatment.

Exclusion Criteria:
- Patients presenting with symptoms sugge-stive of pelvic or lower genital tract infection will be excluded from the study to avoid spread of inflammation.
- Patients with history of hormonal therapy or medical causes of abnormal uterine bleeding such as disorders of coagulation, hypothyroidism or hyperthyroidism will be excluded.
- Cardiac patients for the fear of pulmonary edema from distention media with hystero-scopy.

Genral Examination
- Weight, height, general appearance.
- Vital data (pulse, arterial blood pressure, temperature and respiretory rate).
- Systemic examination including neurolo-gical, full urological, cardiac and chest examination.

Local (vaginal) examination:
Inspection:
- Inspection of the external genital organs for any pathology or vaginal discharge.
- Detection of vaginal or uterine prolapse.

Digital palpation:
- Palpation of the vaginal walls and the cervix for any pathology such as cervical polyp.

Bimanual examination:
To detect the size and the position of the uterus and any pelvic pathology such as fibroid or ovarian cysts.

MRI Examination
(١) Patient preparation
Before MRI examination, the patients were routinely questioned about any of the conditions which might be a contraindication for MRI examination such as cardiac pace makers, metallic intracranial or thoracic surgical clips and metallic prosthetic implants [especially ferromagnetic hip prosthesis]. The patients were instructed to remove any metal object [e.g. jewelry, hair pins] and change into a cotton gown for examination.

MR image analysis
The MR images were evaluated, then correlated with the surgical and pathological findings.

The images were interpretated for
In uterine lesions, site of origin (corporeal or cervical), zonal distribution, lesion size, lesion shape and signal characteristics were determined.

Hysteroscopic Examination
Diagnostic hysteroscopy is carried out to all patients under general anesthesia by a single experienced operator who is blinded to the ultrasound findings.

The hysteroscopy used in this study was Karl Storz (Germany). It is a rigid ٣٠٠ hysteroscope and a ٥mm diameter sheath.

The light source used in this study was a metal halide automatic light source from Circon Acmi G٧١A/Germany with a ١٥٠ Watt lamp. A fibroptic cable is connected to the light source and to the hysteroscope.

Steps Of The Procedure:
- The patient is put in the lithotomy position
- Complete aseptic technique by cleaning the area around the vulva, vagina and the cervix with a non foaming aseptic solution.
- Emptying of the bladder by a metal catheter.
- Examination under anesthesia.

Results

This study included ٤٠ postmenopausal women who had uterine causes of PMB. The age of the studied patients ranged from ٥٠-٧٠ years (mean of ٥٨.٨± ٦.٤ years). Out of them, ٢٨(٧٠٪) had age ≤٦٠ years old, and ١٢(٣٠٪) had age >٦٠ years old. The age of attaining menopause was ٥٠-٥٥ years in ٢٢ patients (٥٥٪), and >٥٥ years in ١٨ patients (٤٥٪). The body mass index (BMI) was <١٨.٥ (underweight) in ٦ patients (١٥٪), ١٨.٥-٢٤.٩ (healthy weight) in ١٠ patients (٢٥٪), ٢٥-٢٩.٩ (over-weight) in ١٦ patients (٤٠٪), and ≥٣٠ (obese) in ٨ patients (٢٠٪).

The parity of the studied ٤٠ patients ranged from ٠-٨ (mean ٣.٦± ٢.٣), and the majority of them were multiparous (٨٠٪). Among the studied ٤٠ patients, there were ٨ (٢٠٪) with diabetes mellitus, ٦(١٥٪) with hypertension, ٤ (١٠٪) with hyperlipidemia and the remaining ٢٢(٥٥٪) had no associated diseases, as shown in (Table ١).

Table ١: Demographic data of the studied ٤٠ women with postmenopausal bleeding.

Variables	Number	Percent
Age at presentation (years):		
≤٦٠	٢٨	٧٠٪
>٦٠	١٢	٣٠٪
Age of attaining menopause (years):		
٥٠-٥٥	٢٢	٥٥٪
>٥٥	١٨	٤٥٪
Body Mass Index:		
<١٨.٥ (Underweight)	٦	١٥٪
١٨.٥-٢٤.٩ (Healthy weight)	١٠	٢٥٪
٢٥-٢٩.٩ (Overweight)	١٦	٤٠٪
≥٣٠ (Obese)	٨	٢٠٪
Parity:		
Nulliparous	٨	٢٠٪
Multiparous	٣٢	٨٠٪
Associated diseases:		
Diabetes Mellitus	٨	٢٠٪
Hypertension	٦	١٥٪
Hyperlipidemia	٤	١٠٪
No associated diseases	٢٢	٥٥٪

Table ٢: Clinical findings by examination of ٤٠ studied patients.

Clinical Findings#	Number	Percent
Tenderness	١٢	٣٠%
Bulky uterus	١٦	٤٠٪
Endocervical polyp	٢	٥٪
Normal	٢٢	٥٥٪

#: More than one finding may be reported in the same patient.
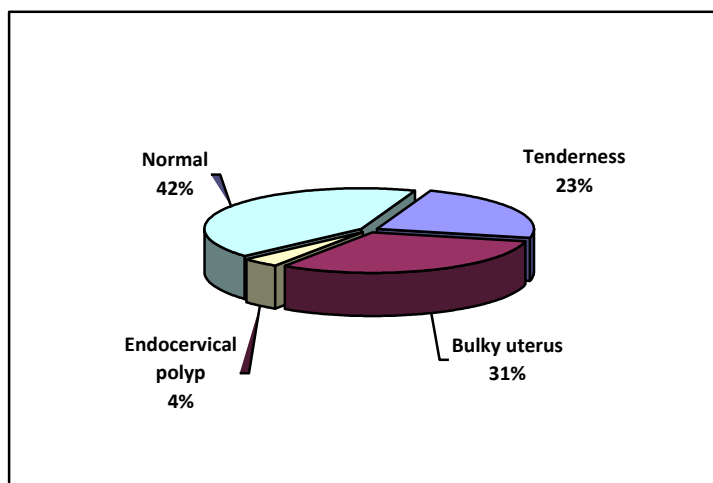
Figure ١: Clinical findings by examination of ٤٠ studied patients**.**

The analyzed risk factors of endometrial carcinoma in ٤٠ studied patients included: age, age at menopause, obesity, parity and comorbidity (Table ٢). There was no significant difference between both groups of age at presentation in relation to presence of carcinoma (P=٠.١١), however the odds ratio was ٤.٣ that means patient >٦٠ years had ٤.٣ times to have endometrial carcinoma more than patients ≤٦٠ years at presentation, which indicates good association between age at presentation >٦٠ years and presence of endometrial carcinoma.

There was no significant difference between both groups of age of attaining menopause in relation to presence of carcinoma (P=٠.٤٧), however the odds ratio was ٢ that means patient with menopause >٥٥ years had ٢ times to have endometrial carcinoma more than patients with menopause ٥٠-٥٥ years old at presentation,

which indicates good association between age of attaining menopause >٥٥ years and presence of endometrial carcinoma.

There was no significant difference between both groups of age of attaining menopause in relation to obesity (BMI ≥ ٣٠), (P=٠.٢٣), and the odds ratio was ٣.٢ that means obese patient had ٣.٢ times to have endometrial carcinoma more than non obese patients, which indicates good association between obesity (BMI ≥ ٣٠) and presence of endometrial carcinoma.

There was no significant difference between both groups of parity in relation to presence of carcinoma (P=٠.٢٣), however the odds ratio was ٣.٢ that means nulliparous patients had ٣.٢ times to have endometrial carcinoma more than multiparous patients, which indicates good association between nulliparous and presence of endometrial carcinoma.

Table ٣: Risk factors of endometrial carcinoma in ٤٠ studied patients.

Risk factor		Carcinoma (N=٥)		No carcinoma (N=٣٥)		Total (N=٤٠)		P-value	Odds Ratio
		No.	%	No.	%	No.	%		
Age	>٦٠ yr	٣	٢٥	٩	٧٥	١٢	١٠٠	٠.١١	٤.٣
	≤٦٠ yr	٢	٧.١	٢٦	٩٢.٩	٢٨	١٠٠		
Age at Menopause	>٥٥	٣	١٦.٧	١٥	٨٣.٣	١٨	١٠٠	٠.٤٧	٢
	٥٠-٥٥	٢	٩.١	٢٠	٩٠.٩	٢٢	١٠٠		
Obesity	High BMI	٢	٢٥	٦	٧٥	٨	١٠٠	٠.٢٣	٣.٢
	Average BMI	٣	٩.٤	٢٩	٩٠.٦	٣٢	١٠٠		
Parity	Nulliparous	٢	٢٥	٦	٧٥	٨	١٠٠	٠.٢٣	٣.٢
	Multiparous	٣	٩.٤	٢٩	٩٠.٦	٣٢	١٠٠		
Comorbidity	Chronic diseases	٢	١١.٢	١٦	٨٨.٨	١٨	١٠٠	٠.٨١	٠.٧٩
	No chronic diseases	٣	١٣.٧	١٩	٨٦.٣	٢٢	١٠٠		

The uterine causes of postmenopausal bleeding as revealed by histopathological examination, hysteroscopy, and MRI of ٤٠ studied patients (in regardless to true or false results), as shown in (Table ٤) and (Fig. ١)

The results of histopathological examination revealed that the uterine causes of PMB were atrophic endometrium in ٢١ patients (٥٢.٥٪), endometrial hyperplasia in ٨ patients (٢٠٪), endometrial polyp in ٦ patients (١٥٪), and endometrial carcinoma in ٥ patients (١٢.٥٪). The staging of the ٥ cases of endometrial carcinoma was stage III in ٣ patients and stage IV in ٢ patients.

Table ٤: The concordance between MRI and histopathological diagnosis of different uterine pathologies in ٤٠ women with PMB.

MRI	Histopathology				Total
	Atrophic endometrium	Endometrial hyperplasia	Endometrial polyps	Endometrial carcinoma	
Atrophic endometrium	١٩	١	٠	٠	٢٠
Endometrial hyperplasia	١	٦	١	١	٩
Endometrial polyps	٠	١	٥	١	٧
Endometrial carcinoma	١	٠	٠	٣	٤
Total	٢١	٨	٦	٥	٤٠

There were insignificant differences in frequencies of different pathological types between histopathology and MRI, as shown in (Table ٨) and (Fig. ٤٢).

Table (٥): Correlation of uterine causes of postmenopausal uterine bleeding as revealed between histopathology and MRI in ٤٠ studied patients.

Causes of bleeding	Histopathology		MRI		P-value
	No.	%	No.	%	
Atrophic endometrium	٢١	٥٢.٥	١٩	١٥	٠.٦٥
Endometrial hyperplasia	٨	٢٠	٦	١٢.٥	١
Endometrial polyps	٦	١٥	٥	٧.٥	٠.٧٦
Endometrial carcinoma	٥	١٢.٥	٣	١٥	٠.٧٢
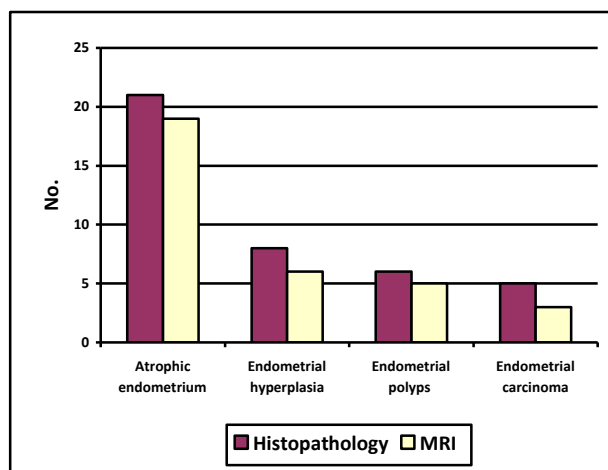
Fig. (٢): Correlation of uterine causes of postmenopausal uterine bleeding as revealed between histopathology and MRI in ٤٠ studied patients.

The true and false results of MRI in diagnosing different pathological causes of PMB are shown in (Table ٩).

Table (٦): Validity of hysteroscopy in diagnosing different pathological causes of PMB.

	Sensitivity	Specificity	PPV	NPV	Accuracy
Atrophic endometrium	٩٥.٢	٩٤.٧	٩٥.٢	٩٤.٧	٩٥
Endometrial hyperplasia	٨٧.٥	٩٦.٨	٨٧.٥	٩٦.٨	٩٥
Endometrial polyps	١٠٠	٩٤.١	٧٥	٩٦.٩	٩٥
Endometrial carcinoma	٨٠	١٠٠	١٠٠	٩٧.٢	٩٧.٥

PPV: positive predictive value. NPV: Negative predictive value.

Discussion

The world health organization (WHO) has defined menopause as the permanent cessation of menstruation resulting from the loss of ovarian follicular activity, thus it is an important phase for dramatic hormone and other changes in lifespan of a woman[٤,٥]. (WHO, ١٩٩٦; Dawood et al., ٢٠١٠).

Postmenopausal bleeding (PMB) is a common problem that affects ١ in ١٠ postmenopausal women older than ٥٥ years[٦,٧]. (Smith-Bindman et al., ١٩٩٨; Dighe, ٢٠٠٩).

The present study included ٤٠ patients who had abnormal uterine postmenopausal bleeding (PMB).

The term postmenopausal bleeding used in the present study refers to an episode of bleeding ١٢ months or more after the last menstrual period other than expected cyclic bleeding that occurs

with sequential hormone replacement therapy (Goldstein et al., ٢٠٠١; Newell and Overton, ٢٠١٢).

The aim of the present study was to estimate the diagnostic accuracy of magnetic resonance imaging (MRI) and hysteroscopy in diagnosis of PMB using histopathological results of endometrial biopsy as a gold standard test.

The principal aim of investigation of PMB is to identify or exclude endometrial pathology, most notably endometrial carcinoma (Campbell et al., ٢٠٠٢). Obtaining endometrial biopsy for histopathological assessment is accurate but it is an invasive procedure than imaging procedures (Breijer et al., ٢٠١٠).

Hysteroscopy is a useful method of the uterine cavity visualisation. Diagnostic hysteroscopy plays a major role in assessing bleeding among postmenopausal women due to its high sensitivity and specificity for diagnosing endometrial lesions. Thanks to localization and elimination of the pathologies like endometrial polyps and intrauterine adhesions the repeated bleeding and the second time admission of the patient for the same reason can be avoided (Wierzbowski et al., ٢٠٠٣; Ribeiro et al., ٢٠٠٧).

Magnetic resonance imaging has a controversy role in diagnosis of uterine causes of PMB. Previous studies showed that the appearances of endometrial cancer, hyperplasia, and benign polyps overlap on MRI and its role is in the staging of biopsy confirmed endometrial cancer. MRI is more sensitive than transvaginal ultrasound or computed tomography in the detection of deep myometrial invasion and tumour spread beyond the uterus (Manfredi et al., ٢٠٠٤; Sahdey, ٢٠٠٧; Ribeiro et al., ٢٠٠٧).

In the present study, the age of the studied ٤٠ patients with PMB ranged from ٥٢-٧٠ years (mean of ٥٨.٨±٦.٤ years). Out of them, ٢٨(٧٠٪) had age ≤٦٠ years old, and ١٢(٣٠٪) had age >٦٠ years old. This finding agrees with the published data in literature which showed that PMB usually occurs between ٥٠ and ٦٠ years of age (Gale and Dey, ٢٠٠٩). In the study by Tandulwadkar et al., (٢٠٠٩), women between ٥٠ and ٥٥ years formed the majority (٥٦.٦٪) of the patients with PMB.

In a large study by Burbos et al., (٢٠١٠), the rate of postmenopausal vaginal bleeding peaks at the age of ٥٥–٥٩ years (٢٥.٩/١٠٠٠ postmenopausal women/year) and declines thereafter. In the present study, the age of attaining menopause in most of was between ٥٠ to ٥٥ years in ٥٥٪ of the studied women, and more than ٥٥ years in ٤٥٪. This finding is attributed to the statement that the age at menopause varies widely amongst women and ranges roughly from ٤٠ to ٦٠ years of age. Diversity in attainment of menopause may be due to regional, community and either variation. Genetic, environmental and nutritional factors also play role (te Velde and Pearson ٢٠٠٢).

In the present study, most of the studied patients were overweight (١٦ patients; ٤٠٪), had BMI between ٢٥ and ٢٩.٩. Similarly, the study by Tandulwadkar et al., (٢٠٠٩) included ٦٠ postmenopausal women (at least ١ year of amenorrhea) with the complaint of PMB, and ٣٠ women (٥٠٪) were overweight. In the present study, the parity of the studied ٤٠ patients ranged from ٠-٨ (mean ٣.٦±٢.٣), and the majority of them were multiparous (٨٠٪).

Similarly, the study by Jillani et al., (٢٠١٠) included ٥٠ women with typical history of PMB. The majority of patients, i.e. ١٦ (٤٨٪) had a parity of ٧ - ٩, ٩ (١٨ %) were nulliparous and ١٢(٢٤٪) patients had parity ١-٣. The study by Sousa et al., (٢٠٠١) concluded that hysteroscopy and ultrasonography were useful screening tests for endometrial carcinoma. Hysteroscopy was a superior diagnostic procedure. For the assessment of endometrial carcinoma, hysteroscopy revealed sensitivity of ٨٨.٩٪, specificity ٩٨.٣٪, positive predictive value ٨٨.٩٪, negative predictive value ٩٨.٣٪.

In the present study, MRI had insignificant difference with histopathological results in diagnosis of different endometrial pathologies in patients with PMB, however MRI sensitivity and overall accuracy were lower than that of hysteroscopy in diagnosis of all diagnosed pathological types on histopathology. For diagnosis of atrophic endometrium, MRI has sensitivity of ٩٠.٤٪, specificity of ٩٤.٧٪, PPV of ٩٥٪, NPV of ٩٠٪, and overall accuracy of ٩٢.٥٪. For diagnosis of endometrial hyperplasia, MRI has sensitivity of ٧٥٪, specificity

of ٩٠٪, PPV of ٦٦.٧٪, NPV of ٩٣.١٪ and overall accuracy of ٨٢.٥٪. For diagnosis of endometrial polyps, MRI has sensitivity of ٨٣.٣٪, specificity of ٩٤.١٪, PPV of ٧١.٤٪, NPV of ٩٦.٩٪, and overall accuracy of ٩٢.٥٪. For diagnosis of endometrial carcinoma, MRI has sensitivity of ٦٠٪, specificity of ٩٧.١٪, PPV of ٧٥٪, NPV of ٩٤.٤ and overall accuracy of ٩٢.٥٪.

In literature, MRI is preferred over computed tomography and ultrasonography in the local staging of gynecological malignancies (Manfredi et al., ٢٠٠٥). MRI can provide valuable data to estimate staging and choose the best treatment planning (Barwick et al., ٢٠٠٦). The treatment of choice for endometrial cancer is surgery. Based on staging, cervical stromal involvement and the depth of myometrial invasion, the type of surgery can differ from a simple hysterectomy without lymphadenectomy or only a lymph node sampling to radical surgery with systematic lymphadenectomy (Kitchener et al., ٢٠٠٩; Zamani et al., ٢٠١٢).

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