Original Research Open Access

Hysteroscopic Findings in Postmenopausal Bleeding and its Correlation with Histopathology: Does Clinical Experience Matter?

Radwa Rasheedy MD, Ahmed Abbas MD
Obstetrics and Gynecology Department; Faculty of Medicine, Ain shams university, Cairo, Egypt.

Abstract

Background: women with PMB have a 10–15% chance of having endometrial carcinoma. Therefore, prompt and accurate evaluation to exclude malignant or premalignant lesions of the endometrium is necessary

Aim: To evaluate different hysteroscopic findings in women with PMB and its correlation with histopathological finding in early and late postmenopausal women.

Methods: This retrospective observational study was carried out in early cancer detection unit (ECDU) in Ain Shams University Maternity Hospital between June 2017 and December 2017 involving medical records of 83 women presented with PMB who underwent hysteroscopy and endometrial sampling. We identified hysteroscopic appearance of the endometrium and any focal lesion then the findings were later correlated with the final histopathological diagnosis.

Results: the commonest hysteroscopic appearance of the endometrium was thick hypertrophic endometrium (59.6% in early postmenopausal years group A and 61.5% in late postmenopausal years group B). Benign pathology was observed in 50 women (87.7%) in group A and in14 women (53.8%) in group B, malignant and premalignant lesions were found in 7% and 30.8% respectively. Inadequate samples occurred in 5.3% and 15.4% of women in group A and B respectively. Hysteroscopic sensitivity in detecting malignant lesions was 83.3%, while its Specificity was 96.87%

Conclusions: Hysteroscopy is an accurate and reliable method for diagnosing endometrial cancers, and offers a good immediate therapeutic option for women with obvious benign lesions as endometrial polyp. There is no difference in hysteroscopic accuracy in detecting malignancy with different operators' clinical experiences.

Keywords: postmenopausal bleeding – Hysteroscopy- operators' clinical experiences

Background

With increasing life expectancy, a healthy 50-year-old woman will spend around 40% of her life in postmenopausal state[1]. Postmenopausal bleeding (PMB) is any abnormal uterine bleeding occurring after at least 1 year of amenorrhea, it accounts for about 5 percent of office gynecology visits .[2] Even a single episode of PMB needs a meticulous evaluation, as it can be the sole manifestation of the underlying endometrial cancer, which may present at a stage when it can be cured completely.[1]

Although, PMB has different causes including endometrial atrophy, polyps, endometrial hyperplasia,

Corresponding Author: **Radwa Rasheedy**: radwaebed@yahoo.com

and endometrial carcinoma.[3] Endometrial cancer can be found in 10%of women with unexpected PMB, depending on age and risk factors (e.g. diabetes, obesity, nulliparous, with late onset of menopause)[4]
Hysteroscopy is a valuable diagnostic tool with high specificity for diagnosing intra-cavitary lesions and endometrial conditions in abnormal uterine bleeding (AUB) evaluation including PMB. [5]

The aim of this study was to evaluate different hysteroscopic findings in women with PMB and its correlation with histopathological findings in early and late postmenopausal women. Another aim was to evaluate the impact of years of clinical experience on accuracy of hysteroscopic diagnosis of endometrial cancer

Methods

The current study was an observational retrospective study during the period from June 2017 to December 2017 involving medical records in the Early Cancer Detection Unit (ECDU) at Ain Shams University Maternity Hospital where office hysteroscopy is performed. Eighty three consecutive women with PMB divided into 2 groups according to the age into (group A included 57 women aged between 50 and 60 years and group B included 26 women aged more than 60 years).

We included every postmenopausal woman older than 50 years complaining of PMB. The parameters of the research were obtained from the case history and hysteroscopy reports retrospectively, and the personnel who performed the procedure were categorized into 3 groups according to the years of clinical experience into three categories(less than one years, two to five years, more than five years of experience)

The histopathological report of each sample retrieved was obtained from the pathology sector in ECDU and were evaluated with correlation the hysteroscopic findings as the histopathological results are considered the gold standard in diagnosing endometrial pathologies.

Hysteroscopically the endometrium was classified into normal, atrophic, thick hypertrophic, polypoidal, suggestive of endometrial carcinoma (obvious intrauterine growth with necrotic tissue and abnormal vascularity). The endometrial vascularity, intracavitary lesions as endometrial polyp or submucous myoma, and any vaginal or cervical pathology that could cause abnormal bleeding were reported

The primary outcome was to study different causes of PMB and how these findings vary in different age groups, while secondary outcomes were the correlation between hysteroscopic findings and histopathological results, the effect of years of experience on the accuracy of hysteroscopic diagnosis, and the reliability of office procedures of obtaining endometrial biopsy.

Statistical Analysis

Analysis of data performed by using SPSS package version 16.0.

Description of data in the form of mean (M) and standard deviation (SD) for all quantitative variables and frequency and percentage for all qualitative variables.
Comparison of qualitative variables was done using chi-square test (X2). Significance levels measured according to P value (probability) $P>0.05$ insignificant, $P<0.05$ significant, $P<0.01$ highly significant. Sensitivity, specificity, and accuracy for detecting endometrial cancer were calculated to assess effect of operators' clinical experiences on hysteroscopic evaluation.

Results

Between June 2017 and December 2017, eighty three women underwent office hysteroscopy for evaluation of PMB in the Early Cancer Detection Unit (ECDU) at Ain Shams University Maternity Hospital and they were divided into 2 groups according to the age into (group A included 57 women aged between 50 and 60 years and group B included 26 women aged more than 60 years).

Table 1 show the demographic and hysteroscopic findings of both groups
The mean age in group A was 52.63±2.57 while in group B was 66.92±4.98, the commonest hysteroscopic appearance of the endometrium was thick hypertrophic endometrium (59.6% in early postmenopausal years and 61.5% in late postmenopausal years).

Table 2 showed the different histopathological finding of the office endometrial biopsy where benign pathology was observed in 50 women (87.7%) in group A and in14women (53.8%) in group B, malignant and premalignant lesions were found in 7%and 30.8% respectively.
Inadequate samples occurred in 5.3% and 15.4% of women in group A and B respectively.

The hysteroscopic sensitivity in detecting malignant lesions was 83.3%, while its Specificity was 96.87% with different sensitivity and Specificity in the three different operators groups according to the years of clinical experience as shown in table 3.

Table 1: demographic and hysteroscopic findings of both groups

Variables		Post-menopausal bleeding		P value
		Early postmenopausal 57	Late Postmenopausal 26	
Age (Y)	Mean± SD	52.63±2.57	66.92±4.98	0.0001*
Hysteroscopic evaluation				
endometrial cavity appearance N(%)	Normal appearance	12(21.1)	2(7.7)	0.25
	Atrophic endometrium	10(17.5)	7(26.9)	
	Thick hypertrophic endometrium	34(59.6)	16(61.5)	
	Bloody field	1(1.8)	0(0)	
Focal lesions N(%)	none	31(54.4)	9(34.6)	0.26
	polypoidal	10(17.5)	3(11.5)	
	Single polyp	11(19.3)	8(30.8)	
	Calcified areas	1(1.8)	1(3.8)	
	Adhesions	1(1.8)	0(0)	
	Hemorrhagic areas	1(1.8)	0(0)	
	mass	0(0)	1(3.8)	
	Necrotic area	2(3.5)	4(15.4)	
Vascularity N(%)	none	43(75.4)	14(53.8)	0.13
	vascular	9(15.8)	7(26.9)	
	Highly vascular	5(8.8)	5(19.2)	
Endo cervical polyp		4(7)	1(3.8)	0.49
Suspicious lesions		4(7)	3(11.5)	0.38

Discussion

Hysteroscopic evaluation of the endometrial cavity has revolutionized the diagnostic and therapeutic methods of endometrial and intracavitary pathologies in the last few decades.[6] The availability of hysteroscopy for guiding endometrial biopsy leads to almost 100% accuracy in the diagnosis of endometrial neoplasia and its precursors.[7] The use of blind endometrial sampling can be inaccurate in diagnosing some pathologies, especially in cases of localized pathologies such as endometrial polyps, submucous myomas, and focal endometrial abnormalities including adenocarcinoma [8]

PMB is a common clinical condition with an incidence of 10% immediately after menopause. [9]the incidence of bleeding appears to decrease over time as reported by Astrup and Olivarius who found that the incidence of bleeding fell from 409/1000 person-years immediately in the first year of menopause to 42/1000 person-years more than three years after menopause.[10]

Also Burbos et al., found that the rate of postmenopausal vaginal bleeding peaks at the age of 55-59 years and declines thereafter.[11] In the current study of the eighty three women presented with PMB 57 of them aged 50 to 60 years and only 26 women were older than 60 years.

We found that the main hysteroscopic appearance in both groups was thickened hypertrophic endometrium (59.6% in early postmenopausal years and in 61.5% in late postmenopausal years) which was followed by endometrial polys in 19.3% and 30.8% and atrophic endometrium in 17.5% and 26.9% of women respectively. In the opposite direction Crispi et al., reported the most common hysteroscopic findings in 507 women with postmenopausal bleeding were endometrial polyps (40.0%) and atrophic endometrium (33.9%). with the histopathological examinations revealed absent material in 47.1%, polyp in 16.4% , atrophy in 5.2%, and endometrial carcinoma in 5.1%. [12]

In the current study different histopathological findings were observed 26.8% of women older than 60 years and 5.3% of women less than 60 years showed endometrial carcinoma, while simple hyperplasia in 11.5% , 26.3% and polyps in 7.7% , 31.6 % respectively.

The average age of diagnosis of uterine cancer in the US is 62 years old with 17 % of cases between 45 to 54 years, 34.5% between 55 to 64, while more than 40% of cases older than 65 years.[13] While in the current study 33.3 % of malignant lesion occurred in women less than 60 years and 66.4% occurred in older women.

Table 2: biopsy findings in both groups:

Variables		Early	Late	pvalue
Endometrial histopathology N(%)	Simple hyperplasia	11(19.3)	3(11.5)	0.004
	Simple hyperplasia with polyp	4(7)	0	
	complex atypical hyperplasia	1(1.8)	1(3.8)	
	complex hyperplasia without atypia	0(0)	1(3.8)	
	secretory endometrium	6(10.6)	1(3.8)	
	proliferative endometrium, with polyp	5(8.8)	0	
	Atrophic endometrium	6(10.6)	3(11.5)	
	cystic atrophic endometrium	0(0)	1(3.8)	
	disordered non proliferative endometrium	4(7)	1(3.8)	
	disordered proliferative endometrium	6(10.6)	0(0)	
	endometrioid adenocarcinoma	2(3.5)	5(19.2)	
	moderate differentiated adenocarcinoma	0(0)	1(3.8)	
	Complex atypical hyperplasia with squamous metaplasia	0(0)	1(3.8)	
	mucinous carcinoma	1(1.8)	0(0)	
	poorly differentiated squamous carcinoma	0(0)	1(3.8)	
	Inadequate sample	3(5.3)	4(15.4)	
cervical biopsy	Endo cervical polyp	3(5.3)	1(3.8)	0.46
	infected endo cervical polyp	3(5.3)	0(0)	
Chronic endometritis		6(10.6)	1(3.8)	0.31
Polyp		18(31.6)	2(7.7)	0.01
Malignancy	Benign	50(87.7)	14(53.8)	0.003
	Malignant/premalignant	4(7)	8(30.8)	
	Inadequate sample	3(5.3)	4(15.4)	

Table 3: effect of physicians 'clinical experience on hysteroscopic findings:

variable	Clinical experience			P value
	less than 1 years	2-5years	More than 5 years	
Number of evaluated cases	37(44.5)	15(18.1)	31(37.4)	
Number of cases with inadequate samples	3(3.6)	1(1.2)	3(3.6)	0.93

	Hysteroscopic assessment for endometrial cancer					
Experience	less than 1 year		2-5 years		More than 5years	
Biopsy	Suspicious	Not suspicious	Suspicious	Not suspicious	Suspicious	Not suspicious
	6	31	4	11	5	25
Malignancy	4	1	3	1	3	0
Benign	1	28	0	10	1	24
sensitivity	80%		100%		75%	
Specificity	96.5%		90.9%		100%	
accuracy	94.11%		92.85%		96.42%	
Over all hysteroscopic sensitivity			83.3%			
Over all hysteroscopic sensitivity			96.87%			

Inadequate sampling was found in 5.3% and 15.4% in early and late menopausal women respectively in the same line Kandil et al., studied the features of endometrial samples designated as insufficient for diagnosis which were more commonly encountered in elderly patients than younger ones (14.6% vs. 5.8%).[14]

Also 20.8% of the 356 women included in Visser et al., study had technically failed sampling, and in 29.8% the amount of tissue was insufficient for diagnosis. Advanced age was associated with insufficient sampling and endometrial thickness >12 mm decreased the chance of insufficient sampling.[15]
In a prospective study performed by Van Doorn et al., four (6%) out of 66 patients with insufficient tissue at office endometrial sample were subsequently diagnosed with endometrial cancer or atypical hyperplasia so women with an insufficient sample should not be reassured.[16]

The incidence of secretory and proliferative endometrium observed to be higher in early postmenopausal years (10.6% and 19.4&) than reported in previous studies[17,18] as progesterone therapy for AUB with hyperplasia is followed by secretory changes of the endometrium [19] and endometrial proliferative activity may occur with uterine prolapse and in endometrial polyps in postmenopausal women.[20]
Garuti and his colleagues found that hysteroscopy imaging can be used to differentiate normal and abnormal endometrium with high accuracy (sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) of 94.2%, 88.8%, 96.3%, and 83.1%, respectively, in predicting normal or abnormal histopathology of endometrium.[21]

The sensitivity of hysteroscopy for diagnosis of endometrial cancer in Crispi et al., study was 93.8%, specificity was 97.7%, and PPV and NPV were 73.2% and 99.6% .[12]
We found that the hysteroscopic sensitivity and specificity in detecting malignant lesions were83.3% and 96.87%. With considering the different operators experience (less than one year, two to five years, or more than five years) the sensitivity and specificity were 80% and 96.5%, 100% and 90.9%, and 75% and 100% respectively).

Clark et al. [22] conducted a systematic quantitative review looking at the accuracy of hysteroscopy in the diagnosis of endometrial cancer and hyperplasia in women with abnormal uterine bleeding. A positive hysteroscopy had a pooled LR of 62.8, whereas a negative hysteroscopy had a pooled LR of 0.15

A study was conducted to assess inter-observer agreement and reproducibility of hysteroscopic diagnosis among experts (>500 hysteroscopies), seniors (20-499 procedures) and junior (less than 20 procedures) gynecologists concluded that sensitivity improves with the observer's experience, but inter-observer agreement and reproducibility of hysteroscopy were not satisfying no matter the level of expertise. [23]
also Di Spiezio Sardo et al., reported that high level of expertise is not a prerequisite to perform hysteroscopy as recent advances in technique and instrumentation facilitate office hysteroscopic procedures and can be adopted by the wider gynecology community. In the same line in our study there were no cases of failed hysteroscopy between different operators; obtaining inadequate sample was comparable in the 3 operator groups (p value 0.93), and hysteroscopic accuracy in detecting highly suspicious lesions was 94.11%,92.85%, and96.42% in operators experience less than one year ,between two and five years, and more than five years respectively.

Strengths and limitations:

A limitation of the present study is the difficulty in evaluating the level of clinical experience of the operator so we had to use years of practicing diagnostic hysteroscopy which is less accurate than number of hysteroscopy per operator, another limitation is being a retrospective study that was performed at a single center on a small sample size.

Conclusion:

Hysteroscopy is an accurate and reliable method for the diagnosis of endometrial cancers, and offers a good therapeutic option for women with obvious benign lesions as endometrial polyp. There is no difference in hysteroscopic accuracy in detecting malignancy with different operators' experiences.

Acknowledgments:

The authors thank the participants of this study.

Disclosure of Interests:

The authors declared no conflicts of interest with respect to the authorship and publication of this article.

Role of the funding source:

No financial support was provided for the conduct of the research or authorship of this article.

References

1 Tandulwadkar S, Deshmukh P, Lodha P, Agarwal B. Hysteroscopy in postmenopausal bleeding. J Gynecol Endosc Surg. 2009; 1(2):89-93.
2 Moodley M, Roberts C. Clinical pathway for the evaluation of postmenopausal bleeding with an emphasis on endometrial cancer detection. J Obstet Gynaecol 2004; 24:736.
3 Sarvi F, Alleyassin A, Aghahosseini M, Ghasemi M, Gity S. Hysteroscopy: A necessary method for detecting uterine pathologies in post-menopausal women with abnormal uterine bleeding or increased endometrial thickness. Turk J Obstet Gynecol. 2016;13(4):183-188.
4 Goldstein, R. B., Bree, R. L., Benson, C. B., Benacerraf, B. R., Bloss, J. D., Carlos, R. , Fleischer, A. C., Goldstein, S. R., Hunt, R. B., Kurman, R. J., Kurtz, A. B., Laing, F. C., Parsons, A. K., Smith-Bindman, R. and Walker, J. Evaluation of the woman with postmenopausal bleeding: Society of Radiologists in Ultrasound-Sponsored Consensus Conference statement.. Journal of Ultrasound in Medicine.2001; 20: 1025-1036.
5 Vardhan S, Mohan S, Ranjan P. HYSTEROSCOPY IN POSTMENOPAUSAL BLEEDING. Med J Armed Forces India. 2011; 57(2):114-6.
6 Pandey D, Kunamneni S, Inukollu PR, Su H. Establishing patterns on hysteroscopy in abnormal uterine bleeding (AUB). Gynecology and Minimally Invasive Therapy .2017;6: 178-182
7 Vardhan MS, Mohan LC, Ranjan MP. HYSTEROSCOPY IN POSTMENOPAUSAL BLEEDING.MJAFI 2001; 57: 114-116.
8 Brill AI. What is the role of hysteroscopy in the management of abnormal uterine bleeding? Clin Obstet Gynecol. 1995;38(2):319-345.

9 Bakour SH, Timmermans A, Mol BW, Khan KS. Management of women with postmenopausal bleeding: evidence-based review. The Obstetrician & Gynaecologist 2012;14:243–9.
10 Astrup K, Olivarius Nde F. Frequency of spontaneously occurring postmenopausal bleeding in the general population. Acta Obstet Gynecol Scand 2004; 83: 203-7
11 Burbos N, Musonda P, Giarenis I, Shiner AM, Giamougiannis P, Morris E, Nieto JJ. Age-related differential diagnosis of vaginal bleeding in postmenopausal women: a series of 3047 symptomatic postmenopausal women. Menopause Int. 2010;16(1):5-8.
12 Crispi, C. P., Vanin, C. M., Dibi, R. P., Kato, S. K., & Pesssini, S. A. Postmenopausal Bleeding: Findings and Accuracy of Hysteroscopy and Histopathologic in the Diagnosis of Endometrial Cancer. Journal of Minimally Invasive Gynecology.2011;18(6):S83.
13 Chen L, Berek JS. Endometrial carcinoma: Epidemiology and risk factors .Post TW, ed. UpToDate. Waltham, MA: UpToDate Inc. http://www.uptodate.com (Accessed on December 02, 2017.).
14 Kandil D, Yang X, Stockl T, Liu Y. Clinical outcomes of patients with insufficient sample from endometrial biopsy or curettage. Int J Gynecol Pathol. 2014 ;33(5):500-6.
15 Visser NC, Breijer MC, Herman MC, Bekkers RL, Veersema S, Opmeer BC, Mol BW, Timmermans A, Pijnenborg JM. Factors attributing to the failure of endometrial sampling in women with postmenopausal bleeding. Acta Obstet Gynecol Scand. 2013;92(10):1216-22.
16 van Doorn HC, Opmeer BC, Burger CW, Duk MJ, Kooi GS, Mol BW. Inadequate office endometrial sample requires further evaluation in women with postmenopausal bleeding and abnormal ultrasound results. Int J Gynecol Obstet 2007;99:100–4.
17 Gon S, Kundu T, Mallick D, Ghosh G. A Study on Histopathological Patterns of Endometrium in Different Types of Abnormal Uterine Bleeding Among Peri And Postmenopausal Women. IOSR Journal of Dental and Medical Sciences. 2016;15 (9): 106-111
18 Sidharth S, Sachchidananda M, Perunkulam J. Management of Proliferative Endometrium on Biopsy in Post-Menopausal Women. Journal of Gynecology and Obstetrics. 2016;4(6) 38-43.
19 Deligdisch L. Effects of hormone therapy on the endometrium. Mod Pathol. 1993;6(1):94-106.
20 McCluggage WG. My approach to the interpretation of endometrial biopsies and curettings. J Clin Pathol. 2006;59(8):801-12.
21 Garuti G, Sambruni I, Colonnelli M, Luerti M. Accuracy of hysteroscopy in predicting histopathology of endometrium in 1500 women. J Am Assoc Gynecol Laparosc. 2001;8(2):207-213.
22 Clark TJ, Voit D, Gupta JK, Hyde C, Song F, Khan KS. Accuracy of hysteroscopy in the diagnosis of endometrial cancer and hyperplasia: a systematic quantitative review. JAMA 2002;288:1610–21.
23 Bourdel N, Modaffari P, Tognazza E, et al. Does experience in hysteroscopy improve accuracy and inter-observer agreement in the management of abnormal uterine bleeding? Surg Endosc. 2016 ;30(12):5558-5564.
24 Di Spiezio Sardo, A., Taylor, A., Tsirkas, P., Mastrogamvrakis, G., Sharma, M., & Magos, A. Hysteroscopy: a technique for all? Analysis of 5,000 outpatient hysteroscopies. Fertility and Sterility.2008; 89(2), 438–443.