

Postmenopausal Bleeding: Incidence of Endometrial Pathology with Endometrial Thickness of 3mm-3.9mm

T. Treacy¹, J. Stokes¹, M. Rochford^{1,2}, M. Barrett^{1,2}, M. Geisler^{1,2}, C. Burke¹.

1. Department of Obstetrics and Gynaecology, Cork University Maternity Hospital.
2. South Infirmary/ Victoria Hospital, Cork.

Abstract

Aim

The aim of this audit was to investigate the prevalence of endometrial hyperplasia or carcinoma in women with PMB whose endometrial thickness measured between 3mm and 3.9mm by ultrasound scan prior to hysteroscopy and endometrial sampling.

Methods

This was a retrospective review of two patient cohorts investigated for PMB at two sister hospitals; Cork University Maternity Hospital and South Infirmary / Victoria Hospital in Cork, Ireland. Patient information and histology reports were reviewed to ascertain this.

Results

42 patients were identified as having PMB and an endometrial thickness between 3mm and 3.9mm on ultrasound examination. Sampling of the endometrium was not performed in 9 cases due to normal hysteroscopic findings. 34 histology reports were reviewed. No case of endometrial hyperplasia or carcinoma was reported.

Discussion

It may be reasonable to omit further investigation in women with PMB and ET <4mm following a normal clinical review, given the low incidence of endometrial pathology in this cohort. There is thus a potential for less investigation without compromising outcomes in women with postmenopausal bleeding using this approach. Studies involving larger patient numbers would lend further support to our data.

Introduction

Postmenopausal bleeding (PMB) is defined as vaginal bleeding occurring 12 months after the permanent cessation of menses due to ovarian failure^{1,2}. It is the most common reason for referral to rapid access gynaecology clinics^{1,3}. Previously, the more invasive investigation of dilation and curettage under general anaesthetic was the main mode of investigation. However, this is gradually being replaced by transvaginal ultrasound scan, outpatient hysteroscopy and endometrial biopsy¹. Transvaginal ultrasound to determine the endometrial thickness (ET) is useful for triaging women with PMB to determine which patients require further tests and which patients can be discharged with reassurance following normal clinical assessment. The thicker the endometrium, the greater the risk of sinister pathology. Endometrial cancer is diagnosed in approximately 10% (5.7-11.5%) of those presenting with PMB, depending on which ET cut-off value is used for further investigation^{1,4}.

Ambulatory, or outpatient, hysteroscopy is an established diagnostic test that is in widespread use in developed countries. It is indicated primarily in the assessment of women with abnormal uterine bleeding, both before and after the menopause. The procedure involves the use of miniaturised endoscopic equipment to directly visualise and examine the uterine cavity, without the need for formal theatre facilities or general or regional anaesthesia. Hysteroscopy allows for visualisation of “macroscopic or focal abnormalities and taking directed biopsies”¹. As hysteroscopy has welcomed smaller diameter hysteroscopes and increased use of vaginoscopy, outpatient hysteroscopy is now widely accepted by women^{1,5}.

In Ireland, the Institute of Obstetrics and Gynaecology Guideline for the Investigation and Management of Postmenopausal Bleeding states that ‘in women not on HRT, an endometrial thickness of less than or equal to 3mm on scan strongly reduces the probability of endometrial pathology’^{1,6}. Therefore, it is usual for women to undergo hysteroscopy, or at least endometrial sampling, if the endometrium measures more than 3mm. There is no Royal College of Obstetricians and Gynaecologists (RCOG) Greentop Guideline specifically for postmenopausal bleeding management. However, it is discussed in the Greentop Guideline for Management of Endometrial Hyperplasia (No. 67).⁷ This guideline highlights that “systematic reviews have suggested a cut-off of 3mm or 4mm for ruling out endometrial cancer and have shown that the probability of cancer is reduced to less than 1% when the endometrial thickness is less than the cut-off.”^{5,7,8} The Scottish Intercollegiate Guidelines Network (SIGN) publication (No. 61) investigating postmenopausal bleeding states that “a cut-off threshold of 3mm or less should be used for TVUS in women with PMB or unscheduled bleeding who have never used HRT”⁹.

Further afield, Australian counterparts recommend a GP surveillance-led follow up for patients with no risk factors in individuals with an endometrial thickness equal or less than 4mm. These patients should only undergo further reassessment with endometrial sampling if there is persistent bleeding¹⁰. From a US perspective, the ACOG (2018) states that “transvaginal ultrasonography is appropriate for an initial evaluation of postmenopausal bleeding if the ultrasound images reveal a thin endometrial echo (less than or equal to 4mm), given that an endometrial thickness of 4mm or less has a greater than 99% negative predictive value for endometrial cancer. Transvaginal

ultrasonography is a reasonable alternative to endometrial sampling as a first approach in evaluating a postmenopausal woman with an initial episode of bleeding”¹¹.

The aim of this audit was to identify women who had a hysteroscopy performed for investigation of PMB with an endometrial thickness between 3 and 4mm. It was considered likely by consultants involved in the PMB services in our units that the incidence of endometrial pathology with ET in this range may be so low that the cut-off for further endometrial assessment could be changed to over 4mm.

Methods

Two patient cohorts were studied as part of two separate audits. Cohort A comprised all women investigated for PMB at the outpatient hysteroscopy clinic at Cork University Maternity Hospital (CUMH) between January 2017 and July 2019. Patients were identified using the hospital appointment management system. Retrospective review of standardised datasheets completed for each patient attending the outpatient hysteroscopy clinic took place. The following variables were analysed, age, BMI, parity, endometrial thickness and histological findings. Data was cross-referenced with clinic letters to identify histology results. Patients with ET between 3 and 3.9mm then analysed as a separate group.

Cohort B included patients with PMB and an ET between 3 and 3.9mm who were investigated by either ambulatory hysteroscopy or hysteroscopy D&C under general anaesthesia at our sister hospital, South Infirmary / Victoria Hospital, Cork between January and December 2018. Information was retrospectively retrieved from the theatre register and electronically-recorded operation notes with reference to subsequent clinic letters for histology results. The following data items were examined in this cohort; age, BMI, parity, endometrial thickness, retrieval of a tissue sample or not following hysteroscopic assessment, histology of removed tissue.

All data was collected in an anonymized fashion and Microsoft Excel (2019, Office 365) was used for analysis.

Results

Table 1: Demographics, cohort A (n=207)

	Median	Inter quartile Range
Age	57	13
BMI (n=200)	29.9	8.3
Parity (n=205)	3	2

Cohort A included 207 women. Median ET was 8mm (ET range 2-30mm). Endometrial thickness was not documented in 35 cases (16.9%). Twenty-one women (10%) had an ET between 3 and 3.9mm.

The mean age of these 21 women was 57.7 years (range 46-85 years). The mean BMI was 27.3 kg/m². Endometrial biopsy was not performed in 4 cases (19%) due to atrophy or normal hysteroscopic findings being seen at hysteroscopy. Tissue samples insufficient for histological analysis were found in 4 cases (19%). The hysteroscopic finding in all of these cases was endometrial atrophy. Overall, there were no discrepancies between histological and hysteroscopic findings. No case of endometrial hyperplasia or malignancy was documented in women with PMB having an endometrial thickness between 3mm and 3.9mm. One case of benign endometrial polyp was detected amongst those with an ET of 3-3.9mm.

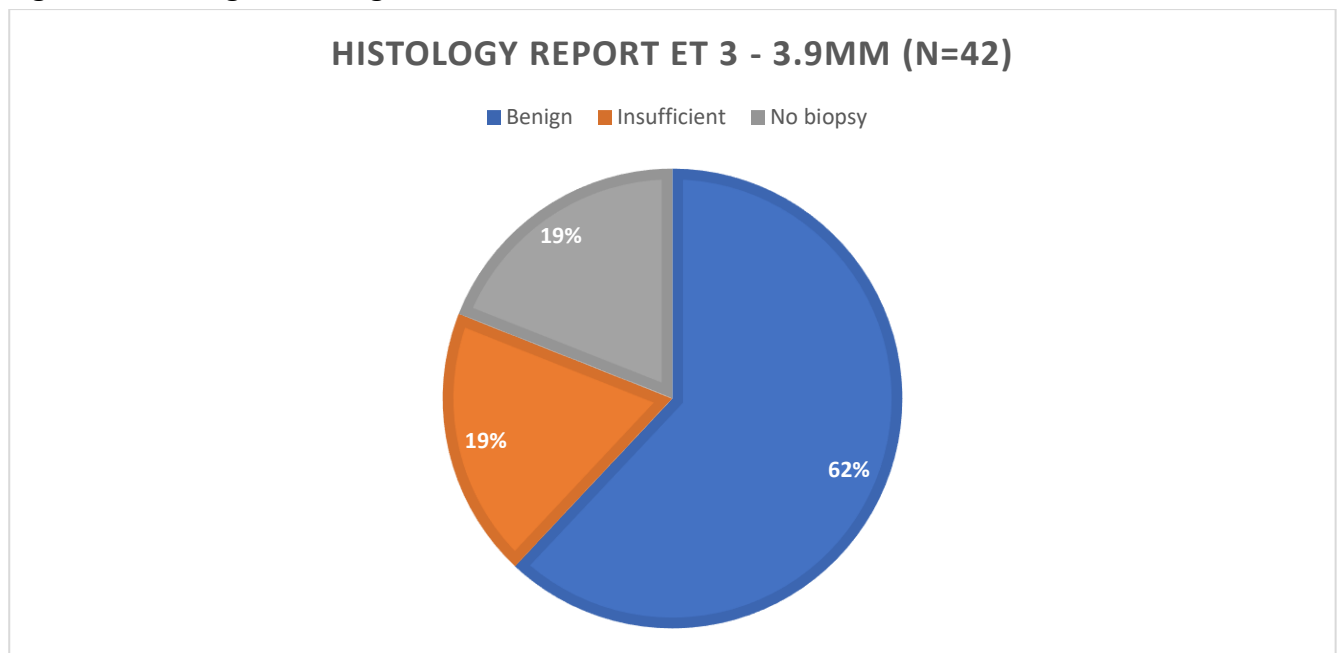
Table 2: Demographics, cohort B (n=21)

	Median	Interquartile Range
Age (n=18/21)	61	16
BMI (n=18/21)	28.5	11.9
Parity (n=18/21)	3	3

Cohort B included 21 women. The average age for this cohort was 62.9 years (range 49-79). The average BMI was 28 (range 20.4-41.9). Tissue was retrieved at the time of endometrial sampling in 17 cases and no tissue was retrieved in 4 cases. Of the 17 endometrial samples obtained, 13 showed benign histology and 4 were insufficient for analysis. One patient in whom endometrial sampling was not achieved later had normal histology post hysterectomy. Three cases of benign endometrial polyp were detected in this cohort, and one benign endocervical polyp was found.

Thus, of 42 women with PMB and ET between 3mm and 3.9mm, no case of endometrial hyperplasia or carcinoma was found. Benign endometrial polyps were found in 9.5% and benign endocervical polyp in 2.4% of cases.

Figure 1: Histological findings in women with PMB and ET 3-3.9mm



Discussion

The overall incidence of uterine cancer in Ireland was 15 per 100,000 women per year between 1994 and 2009¹². Ireland has similar incidence rates to the rest of Europe and ranks 12th highest out of 30 European countries¹³. To date, research employing economic modelling to assess PMB investigation strategies has focused on prevalence^{12,14,15}. The conversation regarding the most appropriate ET cut-off which should prompt further investigation in women with PMB is not new within gynaecology¹⁶. A meta-analysis by Timmermans et al.⁸ in 2010 recommended a cut-off of 3mm with a sensitivity for excluding endometrial cancer of 98%. Russell et al.¹⁶ showed that the lower the ET cut-off for investigation, the more biopsies completed, and the more malignancies identified. There is a cost of these investigations though, both financially for the institution, and physically and psychologically for the patient. Hysteroscopies performed to investigate PMB at lower ET values may be unnecessary, expensive, and potentially harmful to the patient.

One in ten women in our study cohort A had an ET between 3 and 3.9mm (n=21). Age and BMI in this group were both lower than the average for all PMB cases, suggesting an increase in ET in women with PMB, advancing age and / or increasing BMI. Most significantly, of the 42 women with PMB and ET <4mm, no case of hyperplasia or malignancy was detected following hysteroscopy and endometrial sampling. Russell et al¹⁶ concluded that a threshold of endometrial thickness equal to or above 4mm ensures the largest number of malignancies are identified with the minimum number of invasive procedures being performed. They found a post-test probability of endometrial cancer of 0.3% with an ET<4mm. Results of our audit support Russell and suggest that it may be reasonable to discharge women with PMB with ET <4mm following normal clinical evaluation in Irish PMB clinics, given the low incidence of endometrial pathology at this endometrial thickness.

Over-investigation in this older patient group, many having high BMI, multiple medical morbidities and anticoagulant use is to be avoided if possible. The fact that just under one in five (19%) histology samples were insufficient for analysis reflects how little endometrial tissue is available for analysis with this threshold for investigation. By increasing the ET threshold for investigation of PMB from 3mm to 4mm and above, reduced numbers of investigations will result, whilst still providing safe clinical care to women with postmenopausal bleeding. These reductions would be seen across PMB clinic numbers, numbers of endometrial biopsies and hysteroscopies performed, and the numbers of histological samples requiring examination. Reducing the number of hospital attendances would give a reduction in days missed from work or other duties. From a psychological perspective, limiting the number of investigations a patient has to undergo can only serve to benefit them. Importantly, by performing fewer investigations in low-risk women, the resources saved could be redirected into more rapid initial assessment and investigation of those with a higher probability of endometrial cancer.

Regarding the mode of investigation of PMB, Marsh et al.¹⁷ analysed the cost of day-case hysteroscopy versus outpatient hysteroscopy within the NHS. Although the initial financial outlay needed to establish an outpatient hysteroscopy is relatively high, the benefits are still great. Outpatient hysteroscopy costs £54 less per patient than the equivalent day case procedure. Although literature regarding financial implications of outpatient hysteroscopy in the Irish context is lacking, multiple publications regarding patient satisfaction with both doctor and nurse-led outpatient hysteroscopy in Ireland show very favourable results¹⁸. High levels of satisfaction among patients attending out-patient hysteroscopy services in centres in Ireland have been reported with up to 93% reporting they would recommend the service to others^{19,20}.

One limitation of this study lies in the relatively small number of cases examined. Assessing more cases with ET less than 4mm and confirming the chance of sinister pathology could form the basis of potential change to clinical practice. Endometrial thickness was not documented in 17% of women (n=35) undergoing ambulatory hysteroscopy for PMB in CUMH. This reflects a lack of attention to documentation in our ambulatory gynaecology clinic and this information will be transmitted to our hysteroscopists.

In conclusion, our study supports the recommendations of guidelines from Australia and the USA regarding the use of an endometrial thickness cut-off of 4mm or above for the further investigation of PMB. These findings should be considered when updating the Irish national guidelines on the investigation of postmenopausal bleeding. Regarding future research, similar work with a larger sample size would further support this. In addition, examining the financial benefits of changing the ET cut-off to above 4mm would provide practical information for the funding of new or existing PMB services.

Declarations of Conflicts of Interest:

None declared.

Corresponding Author:

Dr Jenny Stokes,
Registrar in Obstetrics and Gynaecology,
Department of Obstetrics and Gynaecology,
Cork University Maternity Hospital.
E-Mail: jestokes@tcd.ie

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