A Clinico-Pathological Study of Transvaginal Endometrial Thickness Measurement in Asymptomatic Postmenopausal Patients and Patients with Postmenopausal Bleeding

Ayse Filiz GOKMEN KARASU[1], Seda ATES[1], Tugba GURBUZ[2], Nurhan SAHIN[3], Taha TAKMAZ[1], Serdar AYDIN[1]

Istanbul, Turkey

ABSTRACT

OBJECTIVE: We aimed to determine the frequency of endometrial pathologies of patients who presented to our outpatient clinic with postmenopausal bleeding and asymptomatic menopausal patients with a finding of thickened endometrium on transvaginal ultrasonography.

STUDY DESIGN: This study was performed at Bezmialem University Hospital. Women who presented to our clinic from January 2015 to January 2017 were analyzed. Patients were divided into two groups. All patients underwent transvaginal ultrasound with a 7.5 MHz probe. Endometrial sampling was performed by either blind dilatation & curettage or pipelle sampling. We excluded patient specimens that were obtained by hysteroscopy.

RESULTS: Electronic records of a total of 368 patients in menopause were inspected. Out of these patients; 287 (78%) underwent endometrium sampling indicated by bleeding. Eighty-one patients (22%) were asymptomatic; however, a thickened endometrium echo on TVUSG examination (≥5 mm) was suspected. The median age was 57 (42-85). In both groups the two leading causes of endometrial pathology was; endometrial polyps followed by proliferative endometrium. The frequency of endometrial cancer was 9.4% for the postmenopausal bleeding group and 1.2% in the asymptomatic patient group.

CONCLUSION: Evaluation of postmenopausal bleeding as soon as possible is essential for diagnosing endometrial pathologies. Role of endometrial thickness is decisive in detecting patients at high risk for malignancy especially with comorbid conditions. Histopathological evaluation is mandatory for ruling out malignancy.

Keywords: Endometrial biopsy, Endometrial thickness, Endometrium cancer, Postmenopausal bleeding

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[1] Bezmialem Vakif University Faculty of Medicine Department of Obstetrics and Gynecology, Istanbul, Turkey.
[2] Medistate Hospital Department of Obstetrics and Gynecology, Istanbul, Turkey
[3] Bezmialem Vakif University Faculty of Medicine Department of Pathology, Istanbul, Turkey

Address of Correspondence: *Ayse Filiz Gokmen Karasu Bezmialem Vakif University Faculty of Medicine Department of Obstetrics and Gynecology, Istanbul, Turkey afgokmen@gmail.com*

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ORCID IDs of the authors:
A.F.G.K: 0000-0001-7480-4691, S.A.: 0000-0003-0472-3727
T.G.: 0000-0003-3555-3767, N.S.: 0000-0002-5039-1164
T.T.: 0000-0003-0793-2348, S.A.: 0000-0002-2043-395X

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Introduction

Postmenopausal bleeding (PMB) indicates any uterine bleeding in a menopausal woman (excluding the expected cyclic bleeding that occurs in women taking hormone therapy). PMB comprises 5 percent of gynecology visits (1). In the early postmenopausal years; the most common etiologies are: endometrial polyps, endometrial hyperplasia and urogenital atrophy (2). With that being said; it is of paramount importance that all postmenopausal women with uterine bleeding should be assessed due to the potential risk attributed to endometrial carcinoma. Approximately 1-4% of postmenopausal patients who attend a doctor with “genital bleeding” will be diagnosed with endometrial cancer (3). These co-dependent factors are; obesity, advanced age, diabetes mellitus and hereditary syndromes (4).

Endometrial adenocarcinoma is the most common gynecological cancer in the world. In 2017 61,380 patients in America were diagnosed with endometrial cancer and 10,920 deaths occurred (1). International guidelines state that the measurement of endometrial echo is the first step to evaluate PMB. TVUSG

can be used as a triage tool to identify women; for blind sampling with either pipelle or dilatation and curettage (D&C) (6).

In this study, we aimed to determine the frequency of endometrial pathologies of patients who presented to our outpatient clinic with postmenopausal bleeding and asymptomatic menopausal patients with a finding of thickened endometrium on transvaginal ultrasonography.

Material and Method

This retrospective cohort study was performed at Bezmialem University Hospital. Consecutive women who presented to our clinic from January 2015 to January 2017 were analyzed using our electronic medical record system. Institutional ethical board approval (number: 19/267-24.10) was obtained. The study was conducted in accordance with the Declaration of Helsinki. Patients were divided into two groups depending on their ICD-10 (International Classification of Diseases) codes: "N.95.0: postmenopausal bleeding" and "N95.9: unspecified menopausal disorder". Menopause was defined as the "cessation of menses for 12 months". All menopausal patients underwent transvaginal ultrasound with a 7.5 MHz probe in a standardized manner (7). Endometrial thickness was measured on a long axis view of the uterus and the maximum anterior-posterior endometrial echo thickness measurement that was obtained was recorded. For asymptomatic women; endometrial sampling was performed equal to and above 5 mm endometrial echo. All women with PMB, regardless of their USG findings underwent histopathological evaluation. Our clinical approach at Bezmialem University is to perform an endometrial sampling to all patients who present with PMB. Endometrium sampling was performed by either blind D&C (dilatation & curettage) or pipelle biopsy. Pathological specimens were examined by specialist pathologists. We excluded patient specimens that were obtained by hysteroscopy.

The patients who underwent endometrium sampling for either PMB or, increased endometrial thickness on ultrasound were analyzed according to their clinical characteristics, transvaginal ultrasonography reports and pathological specimen reports.

All statistical analyses were performed by SPSS (Statistical Package for the Social Sciences) version 21.0 (IBM Corp, Armonk, NY, USA) statistical software. Descriptive statistics were presented as mean and standard deviations for continuous variables. For categorical variables; frequency and percentage were given. Distribution of data was assessed with histogram analysis. Student's t test and Mann Whitney U test were used for the comparison of continuous variables; χ^2 and Fisher's exact tests were performed to compare categorical variables. A p value of <0.05 was considered significant for all tests.

Results

Electronic records of a total of 368 patients in menopause were inspected. Of these 368 subjects; 287 (78%) underwent endometrium sampling indicated by bleeding. Eighty-one patients (22%) were asymptomatic. The median age was 57 (42-85). The median time onset since menopause was 10.6 (± 8.9) years. One hundred and fifty patients (40.8%) had hypertension, 81 patients had diabetes mellitus (22%), 35 patients (9.5%) had a diagnosed thyroid disorder. Twenty patients (5.4%) had a smoking history.

The frequency of different endometrial pathologies and associated TVUSG endometrium echo thickness is demonstrated in table I. The endometrial echo was thickest (14 mm) when the pathology report was either "endometrium cancer" or "atypical endometrial hyperplasia". The median TVUSG endometrium echo was thinnest (6 mm) in cases associated with "insufficient material" and "cervical cancer".

In the PMB group, the most common pathology was endometrial polyp followed by proliferative endometrium. The third most common pathology was "endometrial cancer".

In the symptomatic patient group, the most frequent pathologies were again endometrial polyp and proliferative endometrium. The 3rd most frequent pathology was: "atrophic endometrium" (Table II).

There were 27 cases of endometrial cancer in the PMB group while there was only 1 case of endometrial cancer in the thickened endometrium group. The frequency of endometrial cancer was 9.4% for the PMB group and 1.2% in the asymptomatic patient group.

Table I: *Endometrial pathology and associated TVUSG endometrial thickness*

Endometrial Pathology (n=368)	Number of Patients (n)	TVUSG Endometrial Thickness*
Endometrial polyp	131	10 (2-34)
Proliferative endometrium	120	7 (2-15)
Atrophic endometrium	18	8.5 (2-19)
Simple endometrial hyperplasia	14	10.5 (6-32)
Atypical endometrial hyperplasia	6	14 (7-20)
Endometrial cancer	28	14 (2-53)
Cervical cancer	5	6 (3-21)
Fibrin, mucus (insufficient material)	46	6 (2-8)

**Values given as median (minimum-maximum)*

Table II: *The distribution of endometrial pathologies*

Endometrial Pathology	Dilatation & Curettage Indication	
	Postmenopausal bleeding n=287 (%)	Thickened endometrium on TVUSG n=81 (%)
Endometrial polyp	100 (76.9)	30 (23.1)
Proliferative endometrium	94 (77.7)	27 (22.3)
Atrophic endometrium	11 (61.1)	7 (38.9)
Simple endometrial hyperplasia	10 (71.4)	4 (28.6)
Atypical endometrial hyperplasia	5 (83.3)	1 (16.7)
Endometrial cancer	27 (96.4)	1 (3.6)
Cervical cancer	5 (100)	0 (0)

Discussion

Our first aim in this study was to evaluate the prevalence of endometrial pathology in specimens of asymptomatic postmenopausal women and symptomatic women with PMB. In total; the most frequent pathologies were endometrial polyps (n=131), proliferative endometrium (n=120) and endometrial cancer (n=28). Forty-six specimens were inadequate for histological examination.

The most common pathological results of women with PMB in the literature is endometrial polyps similar to our study. (8-11). It is important to investigate all women who present with PMB to rule out malignancy. In our present study, the frequency of endometrial cancer was 9.4% for the PMB group and 1.2% in the asymptomatic patient group. Depending on the presence of individual patient characteristics such as; old age, body mass index, presence of diabetes, frequency and total time of bleeding; endometrial cancer frequency rises (12,13). In a study conducted by Astrup et al; of 271 postmenopausal women; the incidence of women with bleeding was strongly correlated with time since menopause (14). In our study, the mean time of menopause was 10 years.

In patients with PMB, a cut-off value of 4-5 mm of the endometrial thickness measured by TVUSG has a 99% negative predictive value of endometrial cancer. If TVUSG is used as the initial step in the evaluation of PMB and measurements less than 4-5 mm are omitted, invasive investigations would be avoided in 40% of women (15,16). In the current literature, an ET of ≥4 mm is the current cut-off above which endometrial sampling is recommended (17). However, Type-2 endometrial cancers (clear cell, papillary serous, mucinous endometrial cancer) cannot be reliably excluded based on TVUSG end thickness (18). Thus we performed endometrial sampling to all patients who presented with PMB. Endometrial cancer was found in 27 out of the 287 patients.

Unlike patients with PMB in whom a TVUSG endometrial thickness of <5mm is accepted as low risk for malignancy, in postmenopausal women without bleeding but with an incidental finding of thickened endometrium, the threshold that separates normal endometrium from a pathology has not been standardized. There is likely a preclinical phase during which some cancers might be detectable prior to the development of symptoms (and thus the rationale for considering biopsy in a woman who is not experiencing vaginal bleeding). In our study out of the 81 patients who underwent endometrial sampling indicated by thickened endometrium there was 1 case of atypical endometrial hyperplasia and 1 case of endometrial cancer. In both cases the endometrial thickness was above 10 mm. Similar to our study in a recently published study which constituted of 1995 asymptomatic postmenopausal patient, all cases of endometrial atypical hyperplasia and cancer had an endometrial echo of ≥10 mm (19). It was interesting to note; (refer to Table I) that the median endometrial thickness for "atypical endometrial hyperplasia" and "endometrial cancer" was both 14 mm. This is of importance as we know from previous studies that prevalence of concurrent endometrium cancer in atypical endometrial hyperplasia patients can be as high as 35-40% (20).

In the studies that evaluate ultrasonography for the diagnosis of endometrial cancer, the results and conclusions have been based on a relatively short follow-up time (21,22). Although initially further investigations may not be ordered if the endometrial echo is less than 5 mm, endometrial biopsy will be necessary if there is bleeding, irregular endometrial thickness or risk factors for endometrial cancer in a specific patient (23-25).

Conclusion

Evaluation of PMB as soon as possible is essential for diagnosing endometrial pathologies. Role of TVUSG endometrial thickness in asymptomatic women is questionable in detecting patients at high risk for malignancy especially with comorbid conditions.

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