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Baseline hysteroscopic assessment of endometrium in asymptomatic postmenopausal women with estrogen receptor-positive breast cancer

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Abstract

Objective: The goal of this study was to evaluate the true prevalence of endometrial pathology in asymptomatic postmenopausal estrogen receptorYpositive (ER-positive) breast cancer patients and to know whether some patients are particularly at risk.

Methods: A preliminary cross-sectional study was carried out with 130 postmenopausal ER-positive breast cancer patients. Before any treatment, diagnostic hysteroscopy and endometrial biopsy were performed in all women. Histopathological findings were considered the gold standard in estimating the prevalence of endometrial disease, which was analyzed according to different risk factors.

Results: Hysteroscopic evaluation was possible in 118 patients (90.7%). Of these patients, 68.6% were older than 60 years, and 51.4% were obese. Endometrial polyps were found in 35 patients (29.6%; 1 polyp with simple hyperplasia), and simple endometrial hyperplasia was found in 1 patient (0.8%), with an overall morbidity of the endometrium of 31.3%. Among all the well-established individual risk factors for endometrial pathology, only patient age, body mass index, and time since menopause were significant predictors of endometrial pathology and/or polyps. There was no statistical difference in the thicknesses of

the endometrial lining, but many patients with an endometrial lining of less than 4 mm had polyps of less than 5 mm.

Conclusions: Asymptomatic postmenopausal women with ER-positive breast cancer have a very high prevalence of baseline subclinical endometrial abnormalities. Therefore, endometrial screening before tamoxifen treatment may be useful in all of these patients, and we believe that it should be performed by hysteroscopy in patients at high risk (obese and older women).

Key Words: Breast cancer Y Postmenopausal Y Endometrial pathology Y Body mass index Y Hysteroscopy.

INTRODUCTION

It is not surprising that breast cancer patients also have a higher risk of endometrial cancer1 because many indi- vidual and environmental risk factors (such as nulliparity, early onset of menarche, late age at menopause, and obesity) are shared by both endometrial cancer and breast cancer.2,3 Tamoxifen (TAM) is a nonsteroidal drug with estrogenic and antiestrogenic properties that is widely used as adjuvant therapy and chemoprophylaxis for estrogen receptorYpositive (ER-positive) breast cancer.4 It exerts estrogenic (proliferative) action in the endometrium of postmenopausal women,5 and its prolonged use has been related to an increased risk of de- veloping endometrial pathology (polyps, hyperplasias, and adenocarcinomas).6-8

Although the American College of Obstetricians and Gynecologists Committee on Gynecologic Practice9 in 2006 statedV based on very large trials (National Surgical Adjuvant Breast and Bowel Project and International Breast Cancer Intervention Study)Vthat screening for endometrial cancer with routine transvaginal ultrasonography (TVUS), endometrial biopsy, or both has not been shown to be effective in asymptomatic women who are using TAM, emerging evidence based on the presence or absence of benign endometrial polyps before ther- apy suggests the existence of high-risk and low-risk groups for the development of atypical hyperplasias with TAM treatment in postmenopausal women.10,11 Cancer risk in endometrial polyps is low (3%-10.7%), and the risk of these polyps becoming malignant after TAM treatment, even in asymptomatic patients, is considerably higher than the risk observed in the general population.12 Thus, there may be a role for the pre-treatment screening of asymptomatic postmenopausal women by TVUS, endometrial biopsy, or progesterone challenge test (PCT)13 in all patients before TAM therapy.

Nevertheless, among studies on endometrial morbidity asso- ciated with TAM intake, few reports have provided a reliable and systematic pretreatment endometrial assessment.6,14<21 In addi- tion, in all studies, TVUS had been used as a screening method, and most of these studies used an endometrial thickness of more than 4 mm as an indicator for hysteroscopic evaluation. Hysteroscopy is the only technique that provides a direct visualization of the uterine cavity and, therefore, is the most reliable method of endometrial disease diagnosis. Currently available hysteroscopes have made it possible for polyp re- moval to be performed as an outpatient surgical procedure with few complications and a high degree of user satisfaction. This has made hysteroscopy the gold standard for diagnosing and treating endometrial polyps.22

On the other hand, although TAM is the most common and first-choice endocrine drug used to treat ER-positive breast cancer worldwide, a new option in postmenopausal women is third-generation aromatase inhibitors (AIs; letrozole, anas- trozole, and exemestane). Current studies found a low rate of emerging endometrial pathology during AI therapy,23 and it has been reported that switching from TAM to exemestane significantly reverses endometrial thickening associated with continued use of TAM.24

Moreover, to the best of our knowledge, no other study has investigated the prevalence of endometrial pathology with systematic hysteroscopy in all of these patients, regardless of ultrasonographic findings. It is very important to determine the presence of endometrial disease in postmenopausal women with ER-positive breast cancer not only because of the po- tential endometrial adverse effects of TAM use but also be- cause of an increased risk of uterine bleeding (which creates a consequent need for many diagnostic tests, subsequent treat- ment, and a high burden of anxiety in women with cancer), making the diagnosis and treatment of endometrial pathology (hyperplasia and polyps) before hormonal treatment a very reasonable option in these patients.

The purpose of our study is to estimate the true prevalence of endometrial pathology in all asymptomatic ER-positive breast cancer patients before any treatment at the moment of their diagnosis and to know in which high-risk patients endometrial hysteroscopic screening could be useful before starting hormone treatment.

METHODS

Inclusion criteria

A cross-sectional study was carried out on 190 post- menopausal women with infiltrating breast cancer who were referred by the Radiology Department of Puerto Real Hospital to our gynecologic unit from January 2008 to September 2011 to undergo breast surgical operation. Before surgical treat- ment, the patients were considered eligible for hysteroscopic endometrial evaluation if they had an ER-positive breast cancer and an intact uterus (no previous TAM, no previous hysterectomy, and no previous endometrial ablation), had not

received or were not receiving any hormonal therapy, had not experienced postmenopausal vaginal bleeding, or had not submitted to endometrial biopsy or diagnostic-therapeutic curettage in their postmenopausal period.

Patients were classified as postmenopausal if they had ex- perienced amenorrhea for 1 year or more and had follicle- stimulating hormone values greater than 40 mIU/mL. In addition, women must be asymptomatic from a gynecologic standpoint, and an informed consent form was obtained from each patient after the nature of the study had been fully ex- plained. The eligibility criteria for the study were met by 130 women. The protocol was approved by the local ethics com- mittee, and this study complied with the guidelines of the Dec- laration of Helsinki and with resolution 196/96 of the National Health Council on Research Involving Human Subjects.25

Methods

Anthropometric parameters and follicle-stimulating hor- mone levels were measured in all women. Obesity was de- fined as a Quetelet index of 30 kg/m2 or higher. A detailed gynecologic history was obtained, and TVUS evaluation of the endometrium was performed. Diagnostic hysteroscopy without anesthesia was performed on each woman before any treatment of her breast cancer was performed, independent of ultrasonographic findings. Hysteroscopy was performed in the outpatient clinic by two experienced gynecologists (D.M.L.L. and R.C.D.) using a 5-mm sheathed hysteroscope (Bettocchi Office Hysteroscope; Karl Storz, Tuttlingen, Germany) and physiological saline as distension medium. Based on pre- viously described criteria,26 endometrial hysteroscopic imag- ing was classified into normal (atrophic endometrium and cystic atrophy) or abnormal (polyps, proliferative endome- trium, and focal or extensive endometrial thickening sugges- tive of hyperplasia or adenocarcinoma) finding.

For cases in which the findings from the hysteroscopic view were consistent with normality or extensive hyperplastic fea- tures, endometrial biopsy was carried out by collecting endometrial tissues blindly from all areas of the endometrial cavity using a Karman suction curettage (Gyneaspir; Euro- gyne) and the samples were then sent for histopathological evaluation. In those cases in which focal endometrial abnor- mality was observed, hysteroscopically targeted sampling was carried out by mechanical instrumentation. Upon a hystero- scopic finding of polyps and based on the hysteroscopist’s judgement, immediate outpatient polypectomy was performed with scissors or with a bipolar electrode (Versapoint Bipolar Electrosurgery System; Ethicon, Somerville, NJ). In cases of polyps larger than 3 cm in diameter, firm endocervical stenosis, or a patient’s inability to tolerate the procedure, a deferred inpatient resectoscopic polypectomy under general anesthesia was accomplished. The polyps were sent for his- tological examination separately from other endometrial

biopsies. The findings were classified according to World Health Organization histopathological criteria.27 This classi- fication is based on the morphological features of glands and stroma in the polyps. Size was estimated by the hysteroscopist using the largest polyp as reference. In some cases of atrophic endometrium found by hysteroscopy, a histopathological spec- imen could not be obtained.

Except for endometrial atrophy, pathological findings were considered as the reference test in estimating the prevalence of endometrial morbidity. Therefore, the gold standard for call- ing something a true endometrial polyp was the histology report. Pathological findings were as follows: polyps, pro- liferative endometrium, simple hyperplasia in polyps, and simple hyperplasia or atypical hyperplasia of the endome- trium. In the case of a hysteroscopic diagnosis of atrophic endometrium, either no material was obtained or histopatho- logical findings were derived from an insufficient, inadequate, or nonspecific endometrial sample, atrophy was established. Endometrial pathology prevalence was analyzed according to different demographic and clinical risk factors.

Statistical analysis

The data were collected and analyzed using SPSS 15.0 for Windows (version 11.5; SPSS, Inc.). The clinical and demo- graphic variables of patients (age, parity, breast-feeding, age at menarche, age at menopause, time since menopause, body mass index [BMI], previous hormone therapy, breast tumor size, and endometrial thickness found at ultrasonography) with and without endometrial pathology were compared in all women. Endometrial abnormalities and the prevalence of endometrial polyps were calculated. Statistical analysis was carried out by calculating frequencies, means, and SDs. W2 test was adopted for a comparison of frequencies, and Student’s t test was used for a comparison of means. Then risk factors associated with endometrial pathology were analyzed. Preva- lence ratios with their respective 95% CIs were calculated using Pearson’s W2 test or Fisher’s exact test to evaluate these risk factors. Statistical significance was set at P G 0.05.

RESULTS

The principal demographic and clinical characteristics of patients are shown in Table 1. Among the initial 190 post- menopausal women who had been diagnosed with breast cancer, 130 were eligible for endometrial hysteroscopic eval- uation, and evaluation was possible in 118 patients (90.7%). In 5 cases (3.8%), the patient refused to provide an informed consent form after having been informed about the procedure, and in 7 of 130 cases (5.3%), hysteroscopy was not possible because endocervical stenosis was present or the patient was unable to tolerate the procedure. Resectoscopic polypectomy under general anesthesia was

required in 15 of 40 (37.5%) hysteroscopic diagnoses of endometrial polyps, which represent 12.7% of the total (15/118).

Hysteroscopic diagnoses compared with pathological find- ings and the efficacy of hysteroscopy in the screening of endometrial pathology (sensitivity, specificity, positive predictive value, and negative predictive value) are shown in Table 2. The pathological investigations performed led to the detection of endometrial abnormalities in 37 cases, among which were 35 cases of polyps (1 case of simple hyperplasia harbored within a polyp), 1 case of simple endometrial hy- perplasia, and 1 case of proliferative endometrium (abnormal for postmenopausal women). Complex atypical hyperplasia or endometrial cancer was not found. The overall prevalence of histological endometrial pathology was 31.3%, 29.6% of which were polyps (Table 3).

When we compared the demographic and clinical param- eters of the 37 patients with endometrial pathology with those of the 81 patients with normal endometrium, only patient age (68.8 T 7.6 vs 62.3 T 8.0 y, P G 0.001), weight (78.6 T 15.9 vs 72.2 T 13.0 kg, P = 0.043), BMI (32.0 T 5.5 vs 29.5 T 5.6 kg/m2, P = 0.04), and time since menopause (18.5 T 8.6 vs 12.6 T 9.1 y, P = 0.001) were significantly associated with the finding of an abnormal endometrium. The general hysteroscopic character- istics of histologically tested polyps include the following: average number and range, 1.32 T 0.74 (1-5); size (of the larg- est), 14.28 T 8.93 mm (2-30); proportion of polyps with a size of less than 5 mm, 8 (22.8%); outpatient polypectomy, 20 of 35 (57.14%); deferred inpatient resectoscopic polypectomy, 15 of 35 (42.85%).

Inherent risk factors for endometrial pathology and others related to breast tumors, nalyzed by calculating the prevalence ratios, showed that among all analyzed parameters (age,BMI, menopause status, time since menopause, pregnancy, age at menarche, age at menopause, previous use of hormone therapy, endometrial thickness, breast estrogen receptor, breast progesterone receptor, and breast tumor size), only age, BMI, time since menopause, and endometrial thickness of 5 mm or more had a significant association. Patients older than 60 years had a 6.60-fold prevalence of endometrial pathology (95% CI, 2.14-20.35); patients with a BMI of 30 kg/m2 or higher had a 2.73-fold prevalence of endometrial pathology (95% CI, 1.01-7.40); those with less than 15 years since menopause had a 0.25-fold prevalence of endometrial abnormalities; and women with an endometrial thickness of 5 mm or more had a 4.14-fold prevalence of endometrial pathology (95% CI, 1.42-12.04; Table 4).

About 54.8% of women older than 60 years and with a BMI of 30 kg/m2 or higher had endometrial pathology versus only 12.5% of women 60 years or younger and with a BMI lower than 30 kg/m_2 (P G 0.001; Table 5).

DISCUSSION

The incidence of asymptomatic endometrial pathology in healthy women is unknown, but it seems to be very high. In asymptomatic postmenopausal women, the incidence varies from 0.6% to 13%,28<30 but no prior studies have provided clear conclusions about the incidence of endometrial abnor- malities in these women. The present study lacks a control group of healthy postmenopausal women that might provide significant data on the background incidence of endometrial abnormalities affecting gynecologically asymptomatic postmenopausal women without breast cancer are lacking. There are few data available on the condition of the endometrium in breast cancer patients before endocrine therapy. These studies found an overall incidence of endometrial pathology affecting about 6.2% to 22.2% of postmenopausal women with breast cancer before the start of TAM intake.6,14,15,18,22,23,31,32 Although most of these studies were performed with blind endometrial biopsy and provided no clear conclusions about the real incidence of endometrial abnormalities (especially about endometrial polyps) in these women with breast cancer.

Our findings of baseline endometrial abnormalities in 31.3% of asymptomatic postmenopausal patients with breast cancer are consistent with high pretreatment abnormality rates affecting 22.2% of patients reported in previous series.29 They are higher than 15.3%, 17.4%, 18.0%, and 18.6% of patients reported in other series6,15,19,20; and are much more than the lower rates of baseline pathology ranging from 3.3% to 13.0% reported by other authors.14–17,31 In two studies,17,33 no endometrial abnormalities were found before the start of TAM administration.

To our knowledge, only one study has reported a prevalence higher (37.26) than our findings of baseline endometrial abnormalities.34 However, this study was performed in postmenopausal and premenopausal patients with breast cancer.

In our series of postmenopausal patients affected by breast cancer and candidates about to receive TAM, we found more endometrial abnormalities (31.3%) than Garuti et al20 (18.6%) and Duffy et al19 (18.0%); however, our patients were more obese (BMI, 30.4 vs 24.8 kg/m^2), and fewer had previously used estrogen plus progestogen therapy (11.8% vs 27.4% and 38.5%). Vosse et al10 detected baseline pathology in only 3.3% of cases in 89 postmenopausal patients, but the authors based the hysteroscopic assessment on an 8-mm sonographic cutoff and only performed four hysteroscopies, whereas all of our patients underwent hysteroscopy.

In postmenopausal women with hysteroscopic evaluation of the endometrium, we found much more baseline pathology than other authors who used even a 4-mm sonographic cutoff for hysteroscopic assessment,14,15,18,19,32 principally by detecting endometrial polyps of less than 5 mm (22.8% of polyps). This is the principal reason why we found a higher prevalence than all other previous studies reported.

Contrary to results published in previous reports,2,14,15,32 in which the incidence of baseline atypical lesions was between 0.7% and 3.8%, we did not find any cases of atypical lesions in this current study of asymptomatic women. There was no endometrial cancer, in accordance with a most important previous study.19 In postmenopausal women, 29.6% of biopsies had insufficient tissue for diagnosis, similar to the studies of Nagele et al35 (32%) and Duffy et al19 (36%). This highlights the difficulty of obtaining accurate histological data in the postmenopausal population. The use of any suction device for endometrial biopsy alone would not provide sufficient information, especially in high-risk women.

Abnormality rates of 30% to 60% were reported in patients who were already undergoing TAM therapy, not taking into account pretreatment findings.36 This prevalence of pathology is only a little higher than the baseline rate of abnormalities detected in the present study, suggesting a general overestimation of drug-induced endometrial morbidity found in studies that did not take into account pretreatment findings.

From a diagnostic point of view, saline contrast sonohysterography (SCSH) is as capable as office hysteroscopy in excluding pathology and could be cheaper, easier, and less painful for patients. On screening, SCSH displays a level of performance similar to that of diagnostic hysteroscopy in detecting focal intrauterine pathology37; both procedures, depending on operator and patient preference, are virtually interchangeable. Gumus et al38 reported that SCSH showed a very good agreement with hysteroscopy in the diagnosis of endometrial abnormalities in asymptomatic postmenopausal women (sensitivity of 88.8% and specificity of 84.4%, vs sensitivity of 91% and specificity of 82% for hysteroscopy).

Although hysteroscopy is the most effective method for the diagnosis and treatment of endometrial disease,19 gynecologically asymptomatic women may find it too invasive. However, women recently diagnosed with breast cancer were very willing and often grateful to be thoroughly examined. In this way, 90.7% of women had successful screening with hysteroscopy and biopsy. The outpatient screening was well tolerated with a failure rate of only 5.3%, similar to the study of Duffy et al,19 which had a success rate of 91% and a failure rate of 4%. This would suggest that hysteroscopy is successful as a technique and that patient acceptability is high even for asymptomatic postmenopausal women.

Endometrial polyps are common, occurring in more than 25% of the general population (symptomatic and asymptomatic premenopausal and postmenopausal women), and most frequently in women during perimenopause and postmenopause.39 We found a hysteroscopic diagnosis of polyps in 33.2% of asymptomatic postmenopausal ER-positive women, and higher than that reported in 2009 by Dreisler et al,30 who found polyps in 13% (22/169) of asymptomatic postmenopausal women.

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In 35 of 40 (87.5%) hysteroscopic diagnoses of endometrial polyps in our postmenopausal women, diagnosis was histo- logically confirmed, representing an acceptable rate of false-positive findings on hysteroscopic screening. This compares favorably with another study with a rate of 62% to 75%,19 and this could be due to the realization of the study by a single observer and a single laboratory.

When we analyzed the risk factors for baseline endometrial pathology or endometrial polyps (Table 4), we found that only a BMI of 30 kg/m2 or higher, time since menopause of 15 years or more, age above 60 years, and an endometrial thickness of 5 mm or more are predictors of endometrial abnormalities; these findings are in accordance with those observed in the general population.12 These results, along with a much higher prevalence of endometrial pathology in postmenopausal ER- positive women older than 60 years who are obese (54.8%) versus women younger than 60 years who are not obese (12.5%; Table 5), lead us to conclude that pretreatment screening is especially necessary in those patients. Various risk factors for endometrial polyps have been identified in patients with TAM treatment, such as older age at menopause, longer duration of breast disease, long-term TAM therapy (948 consecutive months), higher body weight, and thicker en- dometrium as measured by TVUS12; however, to our knowl- edge, there is no study similar to ours that analyzes these risk factors before use of TAM.

Only age, menopause status, and postmenopausal bleeding have been identified as factors associated with malignancy in endometrial polyps.42 With respect to age, Antunes et al42 and, more recently, Costa-Paiva et al43 from the same group confirmed that women older than 60 years have a prevalence of premalignant or malignant polyps 5.31 times greater than women aged 40 to 59 years. Hileeto et al44 also found a strong association between age and malignancy in endometrial pol- yps, reporting 32% of malignant polyps in a group of women older than 65 years compared with 7.2% in women aged 25 to 65 years. Advanced age and menopause status have also been identified in other studies as predictors of malignancy in endometrial polyps.45,46 It is important to note that the pres- ence of abnormal bleeding, either during menopause or in perimenopause, was not found to be a risk factor for pre-

malignancy or malignancy in the studies carried out by Savelli et al45 and Ben-Arie et al,47 although Costa-Paiva et al43 found a higher prevalence of malignancy in endometrial polyps in women with postmenopausal bleeding (prevalence ratio, 3.67; 95% CI, 1.69-7.97).

In relation to the effect of TAM, endometrial polyps are the most common endometrial pathology described in association with postmenopausal use, with an incidence of 8% to 36%.12 Bergman et al48 observed that, in users of this drug and with a higher incidence of endometrial polyps, there was also a greater association of these polyps with carcinomas of a more aggressive histological type and grade. Cohen49 reported that the rate of malignancy reported in endometrial polyps recovered from postmenopausal breast cancer TAM-treated patients is much higher than that in the general population (from 2.0% to 10.7%) and that no specific clinical features (including patient age and frequency of postmenopausal bleeding) are associated with these malignant polyps.

To date, the indications for polypectomy have not been agreed upon, especially for premenopausal and asymptomatic women.12 In TAM-treated patients, the risk factors for the development of atypical endometrial lesions are obesity, prior exposure to unopposed estrogens, and endometrial polyps di- agnosed at basal screening (11.7% vs 0.7% without previous polyps).11,15,50 For all these factors and because removal of the polyps is the only way to rule out malignancy, we believe that pretreatment polypectomy is necessary in postmeno- pausal women with ER-positive breast cancer.51 Furthermore, we believe that polypectomies could be performed in all of these women to decrease anxiety and the number of diagnos- tic tests in the case of abnormal bleeding.

In the Intergroup Exemestane Study,52 the Breast Interna- tional Group 1-98 trial,53 and the new Tamoxifen Exemestane Adjuvant Multinational study,54 treatment of postmenopausal women with third-generation AIs (exemestane or letrozole) was associated with a lower incidence of endometrial abnor- malities compared with sequential treatment (TAM followed by AIs).

Thus, as many authors have cited,20,32,55-57 we believe that there may be a role for pretreatment screening in post- menopausal women with ER-positive breast cancer. We rec- ommend this to be performed by TVUS, SCSH, or PCT13 in all patients, and by outpatient hysteroscopy in high-risk women (obese women and women older than 60 y) because it would be beneficial to diagnose and treat endometrial path- ology before treatment with TAM is started, or to evaluate AI treatment with a lesser effect on the endometrium.

CONCLUSIONS

In summary, our results demonstrate a very high prevalence of occult endometrial pathology in asymptomatic postmenopausal women with ER-positive breast cancer before any

treatment. This prevalence is higher than those in previous reports based on a nonhysteroscopic systematic endometrial investigation. From these results, we believe that an endome- trial assessment based on TVUS, SCSH, or PCT screening is always recommended before hormonal therapy is started, and that hysteroscopic basal assessment may be performed in high-risk (older and obese) women for the diagnosis and treatment of the highly prevalent endometrial polyps.

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Tables

Table 1. Demographic and clinical characteristics of patients

Variable	PM-ER+ patients (n = 118)
Age, y	64.5 ± 8.2 (47–84)
Age ≥60 y, %	68.6
Body mass index, kg/m²	30.4 ± 5.7 (18.7–43.7)
Obesity prevalence, %	51.4
Pregnancy	3.6 ± 2.0 (0–11)
Parity	3.1 ± 1.8 (0–9)
Age at menarche, y	12.6 ± 1.6 (9–17)
Age at menopause, y	49.6 ± 4.6 (34–60)
Time since menopause, y	14.7 ± 9.3 (1–37)
Endometrial thickness, mm	4.0 ± 2.8 (0–15)
Endometrial thickness ≥4 mm, %	30.6
Previous HT, %	11.8
Breast-feeding, %	70.6
Breast tumor size, mm	21.7 ± 13.6 (5–90)
Progesterone receptor–positive breast cancer, %	75/96 (78.1)

Values are expressed as mean ± SD (range) or as absolute number and its frequency.
PM-ER+, postmenopausal estrogen receptor–positive breast cancer patients; HT, hormone therapy (use before 1 y).

Table 2. Correlation between endometrial hysteroscopic and histopathological findings and efficacy of hysteroscopy on the screening of endometrial pathology

Histology (Hysteroscopy)	Atrophic endometrium	Insufficient specimen	Cystic atrophy	Secretor endometrium	Proliferative endometrium	Endometrial polyp + secretor endometrium	Endometrial polyp + proliferative endometrium	Endometrial polyp + atrophic endometrium	Simple hyperplasia in polyp	Simple endometrial hyperplasia	Atypical endometrial hyperplasia	Total
Atrophic endometrium	41	28[a]	1	0	0	0	0	0	0	0	0	70
Cystic atrophy	0	2	4	0	0	0	0	0	0	0	0	6
Secretor endometrium	0	0	0	0	0	0	0	0	0	0	0	0
Proliferative endometrium	0	0	0	0	0	0	1	0	0	0	0	1
Endometrial polyp + secretor endometrium	0	0	0	0	0	0	0	0	0	0	0	0
Endometrial polyp + proliferative endometrium	0	0	0	0	1	0	7	0	1	0	0	9
Endometrial polyp + atrophic endometrium	0	5	0	0	0	0	0	26	0	0	0	31
Endometrial hyperplasia	0	0	0	0	0	0	0	0	0	1	0	1
Total	**41**	**35**	**5**	**0**	**1**	**0**	**8**	**26**	**1**	**1**	**0**	**118**

Efficacy of hysteroscopy, %:

Sensitivity (Se): 100;
Specificity (Sp): 93.8;
Positive predictive value (PPV): 88.09;
Negative predictive value (NPV): 100.

[a] In 28 women with hysteroscopic diagnoses of atrophic endometrium, no material or insufficient specimen was obtained by biopsy, and these cases were finally catalogued as atrophic endometrium for purposes of analysis.

Se, sensitivity; Sp, specificity; PPV, positive predictive value; NPV, negative predictive value.

Table 3. Hysteroscopic and histological diagnoses

		PM-ER+ patients (n = 118), n (%)
Method	**Diagnosis**	**n (%)**
Hysteroscopy	Endometrial pathology	42 (35.59)
	Endometrial polyps	40 (33.89)
Histology	Endometrial pathology	37 (31.35)
	Endometrial polyps	35 (29.66)

Values are expressed as absolute number and its frequency.
PM-ER+, postmenopausal estrogen receptor–positive breast cancer patients.

Table 4. Risk factors associated with endometrial pathology in asymptomatic postmenopausal estrogen receptor–positive breast cancer patients: prevalence ratio

Factor	With endometrial pathology, %	Without endometrial pathology, %	P[a]	Gross PR (relative risk)	95% CI
Age, y (n = 118)					
<60	10.8	89.2	<0.001	1.00	2.14–20.35
≥60	44.4	55.6		6.60	
BMI, kg/m² (n = 72)					
<30	25.7	74.3	0.045	1.00	1.01–7.40
≥30	48.6	51.4		2.73	
Time since menopause, y (n = 118)					
<15	22.7	77.3	0.001	0.25	0.11–0.58
≥15	53.2	46.8		1.00	
Pregnancy (n = 116)					
<3.5	32.8	67.2	0.675	0.84	0.39–1.83
≥3.5	36.5	63.5		1.00	
Age at menarche, y (n = 109)					
<12.5	39.6	60.4	0.223	1.00	0.27–1.35
≥12.5	28.6	71.4		0.61	
Age at menopause, y (n = 118)					
<50	38.3	61.7	0.488	1.00	0.34–1.65
≥50	32.1	67.9		0.76	
Endometrial thickness, mm (n = 107)					
<4	29.9	70.1	0.101	1.00	0.86–4.89
≥4	46.7	53.3		2.05	
Endometrial thickness, mm (n =					

Factor	With endometrial pathology, %	Without endometrial pathology, %	P[a]	Gross PR (relative risk)	95% CI
107)					
<5	27.5	72.5	0.006	1.00	1.42–12.04
≥5	61.1	38.9		4.14	
Previous HT use (n = 34)					
No	26.7	73.3	0.943	1.00	0.08–10.1
Yes	25.0	75.0		0.91	
Breast progesterone receptor (n = 96)					
PR−	42.9	57.1	0.295	1.00	0.21–1.59
PR+	30.7	69.3		0.59	
Breast tumor size, mm (n = 118)					
<25	26.8	73.2	0.166	0.54	0.23–1.29
≥25	40.0	60.0		1.00	

The significance of values in boldface was established as $P < 0.05$.
PR, prevalence ratio; BMI, body mass index; HT, hormonal therapy.
[a] Pearson's χ^2 test or Fisher's exact test.

Table 5. Endometrial pathology in older and obese women

PM-ER+ (72/118)

Group	With endometrial pathology, n (%)	With endometrial pathology, %	Without endometrial pathology, %	P
Older + obese[a]	31 (43.0%)	54.8	45.2	<0.001
Older + not obese[b]	19 (26.3%)	36.8	63.2	<0.001
Not older + obese[c]	6 (8.3%)	16.7	83.3	<0.001
Not older + not obese[d]	16 (22.2%)	12.5	87.5	<0.001

PM-ER+, postmenopausal estrogen receptor–positive breast cancer patients.

[a] Sixty years or older and body mass index of 30 kg/m² or higher.
[b] Sixty years or older and body mass index lower than 30 kg/m².
[c] Younger than 60 years and body mass index of 30 kg/m² or higher.
[d] Younger than 60 years and body mass index lower than 30 kg/m².

The values in bold highlight the difference in the endometrial pathology incidence between the obese and the older than 60 groups and the group of women younger than 60 years and BMI lower than 30.