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Endometrial polyps: when to resect?

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Abstract
Purpose To determine the prevalence of malignant and premalignant endometrial polyps and to investigate the association of malignancy with specific factors.
Methods This is a retrospective study of women submitted to hysteroscopic resection of endometrial polyps between January 2005 and July 2013 at a university hospital in southern Brazil. Data regarding clinical characteristics and pathology findings were collected from patient charts.
Results Of 359 patients, 87.2 % had benign polyps and 9.9 % had hyperplasia without atypia. Atypical hyperplasia was found in 2.6 % of the sample. Endometrial adenocarcinoma was found in one woman (0.3 %). A correlation was observed between malignant/premalignant polyps and patient age, menopausal status, and uterine bleeding. All patients with malignancies/premalignancies had abnormal uterine bleeding. Higher frequency of malignant polyps was observed in tamoxifen users, however, without statistical significance ($p = 0.059$ %). Malignancy was not correlated with arterial hypertension, diabetes mellitus, obesity, hormone therapy, endometrial thickness, and polyp diameter.
Conclusions Malignant/premalignant findings had low prevalence and were absent in asymptomatic patients. From the data of this retrospective study, it is unclear whether routine polypectomy should be performed in asymptomatic patients. Further prospective studies including larger numbers of patients are required to guide treatment recommendations.

Keywords Endometrial polyps · Hysteroscopy · Malignancy · Menopause · Uterine bleeding

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Introduction

Endometrial polyps are overgrowths of stroma and glands that project into the uterine cavity. Even though they are usually asymptomatic, endometrial polyps may cause abnormal uterine bleeding. In women experiencing abnormal bleeding, the prevalence of endometrial polyps ranges from 13 to 50 % [1]. However, because these polyps are usually asymptomatic, their actual prevalence in the general population remains unknown. Also, the pathogenesis of endometrial polyps has not been elucidated. Nevertheless, there is evidence of a genetic basis linked to changes in chromosomes 6 and 12 [2]. Other studies have shown that changes in protein p63 expression [3], the presence of estrogen and progesterone receptors [4], and endometrial aromatase expression all play a role in the pathogenesis of endometrial polyps [5].

The literature shows that endometrial polyps are associated with endometrial hyperplasia and carcinogenesis [6], with a reported prevalence of malignant and premalignant lesions ranging from 0 to 12.9 % [6–12]. The role of several factors—including menopausal status, age, obesity, hypertension, use of hormone therapy or tamoxifen, polyp diameter, and presence of symptoms (most notably abnormal bleeding) [8, 11, 13, 14]—in premalignant and malignant

transformation has been considered, with conflicting results. In addition, some well-known risk factors for endometrial cancer have also been associated with the presence of endometrial polyps, such as older age and obesity [15].

The widespread use of transvaginal ultrasound has led to an increase in the number of endometrial polyps detected in both symptomatic and asymptomatic patients, and routine polypectomy has become a matter of debate [7, 10, 16]. Even though performed in an outpatient setting, hysteroscopic polypectomy, the surgical treatment of choice for endometrial polyps, is associated with cost, need for trained professionals, and, as with all surgical procedures, some degree of risk.

The aim of the present study was to determine the prevalence of malignant and premalignant lesions in women with an ultrasound diagnosis of endometrial polyps submitted to hysteroscopic polypectomy, as well as to investigate the association of malignant and premalignant transformation with risk factors described in the literature (age, menopausal status, uterine bleeding, use of hormone or tamoxifen therapy, obesity, hypertension, diabetes mellitus, polyp size, and endometrial thickness).

Methods

This retrospective study included all hysteroscopic procedures for resection of endometrial polyps performed between January 1, 2005 and July 30, 2013 at a university hospital (Hospital de Clínicas de Porto Alegre, HCPA) in Brazil, and whose data were available from the institution's surgical database.

Data regarding age, body mass index (BMI), menopausal status, use of hormone or tamoxifen therapy, systemic hypertension (SH), diabetes mellitus (DM) as well as ultrasonographic findings of endometrial thickness and suspected endometrial polyps were collected from the patients' charts. Women who had been amenorrheic for at least 12 months were categorized as postmenopausal. Abnormal uterine bleeding was defined as any postmenopausal bleeding or premenopausal bleeding that was different from the usual pattern.

Hysteroscopic resections were performed under general anesthesia with a 10 mm, 30° Hamou hysteroscope. The uterine cavity was distended with mannitol. The cervical canal and the endometrial cavity were examined. All lesions were hysteroscopically resected using a monopolar cautery hook.

Histological evaluation was performed by a pathologist according to institutional protocols. Polyps were classified as benign (functional, non-functional or atrophic, hyperplastic without atypia), premalignant (with simple or complex atypical hyperplasia), or malignant (endometrial carcinoma).

The protocol was approved by the HCPA research ethics committee. Signature for informed consent form was not required given the retrospective nature of the study.

Statistical analysis

Quantitative variables were described as means and standard deviation or median and interquartile range. Qualitative variables were described as absolute or relative frequencies. Student's t test was used to compare group means. In case of asymmetry, Mann–Whitney test was used. To compare group proportions, Pearson's Chi square or Fisher's exact test were employed. Sensitivity, specificity, positive and negative predictive values were calculated. Significance was established at 5 % ($p \leq 0.05$). All analyses were carried out using SPSS 18.0.

Results

We analyzed data from 359 women submitted to hysteroscopic polypectomy. The mean age of patients was 53.0 ± 11.7 years (mean ± SD), and 178 (51.4 %) were postmenopausal. Among postmenopausal patients, the median time since menopause was 132 months (interquartile range 60–231 months). The frequency of abnormal bleeding was 77.38 % in premenopausal patients and 64.6 % in postmenopausal patients, with an overall frequency of 70.8 %. The demographic characteristics of the sample are described in Table 1.

Benign polyps were identified in 87.2 % of the cases (Fig. 1). Endometrial hyperplasia without atypia was found in 33 patients (9.9 %), atypical hyperplasia in 9 patients (2.6 %) and endometrial carcinoma in 1 patient (0.3 %). The patient diagnosed with endometrial carcinoma came to the HCPA emergency room with ascites and pleural effusion from carcinoma of unknown primary site. Hysteroscopy was performed and the pathology diagnosis was polypoid adenocarcinoma. In five cases (1.39 %), the histologic result was not available because the procedure was stopped before excision of the lesion (one cardiorespiratory arrest during anesthesia induction and four perforations identified at the start of hysteroscopy).

Regarding the evaluation of factors potentially associated with endometrial malignancy, a statistically significant difference was observed between the groups with and without malignancy in menopausal status, age and presence of bleeding. In ten patients with malignant and premalignant findings, nine (90 %) were postmenopausal vs. 168 (51.1 %) of 342 patients with benign polyps ($p = 0.021$).

Table 1 Characteristics of the sample

Characteristic	*N*	%
Menopausal status		
Postmenopausal	178	51.4
Premenopausal	168	48.6
Obesity (BMI > 30)	168	51.9
SH	165	46
DM	49	13.6
Use of tamoxifen	32	9.3
Use of HT (E + P)	28	8.1
Use of HT (E)	2	0.6
Abnormal premenopausal bleeding	130	37.8
Age	53 ± 11.7	
Mean ± SD/median (25–75 percentile)		
Months since menopause	132 (60–231)	
BMI (kg/m^2)	30.3 ± 6.6	
Endometrial thickness (mm)	11 (8–15)	
Polyp size (mm)	13 (10–18)	

BMI body mass index, *DM* diabetes mellitus, *HT (E)* estrogen hormone therapy, *HT (E + P)* combined estrogen and progesterone hormone therapy, *SH* systemic hypertension

* Continuous variables expressed as means ± standard deviation or median (25–75 percentile)

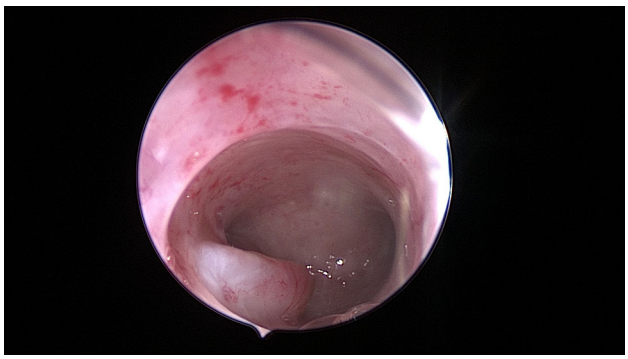

Fig. 1 Hysteroscopic image of a benign polyp in an asymptomatic postmenopausal patient

All patients with malignant or atypical findings had bleeding; in contrast, premenopausal bleeding was observed in 73.9 % s ($p = 1.00$) and postmenopausal bleeding in 65.1 % ($p = 0.031$) of those with benign polyps. The mean age was 64.7 ± 10.7 years for patients with malignant and premalignant lesions and 52.7 ± 11.6 years for women with benign lesions ($p = 0.001$) (Table 2).

The evaluation of bleeding as a predictor of malignant or premalignant lesions revealed sensitivity of 100 % (95 % CI = 72.25–100 %), specificity of 29.67 % (95 % CI = 25.05–34.76 %), negative predictive value of 100 % (95 % CI = 99.46–100 %) and positive predictive value of 4 % (95 % CI = 2.22–7.29 %).

Table 2 Association between malignancy and study variables

Variable	Malignant/ premalignant lesions ($n = 10$)	Benign lesions ($n = 342$)	
Age (years)	64.7 ± 10.7	52.7 ± 11.6	0.001
Menopausal status			0.021
Pre	1 (10.0)	161 (48.9)	
Post	9 (90.0)	168 (51.1)	
Months since menopause	228 (138–282)	120 (57–228)	0.105
BMI (kg/m^2)	32.6 ± 6.4	30.3 ± 6.7	0.348
Obesity	4 (50.0)	160 (51.6)	1.000
Comorbidities			
SH	6 (60.0)	158 (46.2)	0.524
DM	2 (20.0)	47 (13.7)	0.636
Endometrial thickness(mm)	15 (11–20)	11 (8–15)	0.086
Polyp size (mm)	26 (26–26)	13 (10–18)	0.087
Previous diagnostic hysteroscopy	8 (80.0)	174 (53.7)	0.118
Tamoxifen use	3 (30.0)	29 (8.8)	0.059
HT (E + P)	2 (20.0)	26 (7.9)	0.197
Bleeding			
Premenopausal	1/1 (100 %)	119/161 (73.9 %)	1.000
Postmenopausal	9/9 (100 %)	108/166 (65.1 %)	0.031
Total	10/10 (100 %)	227/327 (69.4 %)	0.037

BMI body mass index, *DM* diabetes mellitus, *HT (E + P)* combined estrogen and progesterone hormone therapy, *SH* systemic hypertension

When the results were grouped according to type of lesion (benign vs. malignant/premalignant), no differences were observed between the groups regarding time since menopause, presence of DMor SH, BMI, endometrial thickness, size of polyp on ultrasound or use of hormone therapy. Malignant/premalignant lesions were more frequent in users of tamoxifen; however, the difference was not statistically significant (30 % for malignant/premalignant vs. 8.8 % for benign, $p = 0.059$). The distribution of benign vs. malignant/premalignant histology between pre- and postmenopausal patients is shown in Table 3.

In 88.6 % of the cases, hysteroscopy was performed without complications (Table 4). The most frequent complication was need for antibiotic treatment (5.6 %), because of uterine perforation/creation of false cervical passage (4.5 %). Antibiotics were used in the treatment of any type of postoperative infection, including pelvic, vaginal, respiratory tract and urinary tract infections, and were prescribed

Table 3 Distribution of benign vs. malignant/premalignant histology between pre- and postmenopausal patients ($n = 352$)

Type of lesion	Premenopausal ($n = 162$)	Postmenopausal ($n = 177$)
Benign	161 (99.4 %)	168 (95.0 %)
Malignant/premalignant	1 (0.6 %)	9 (5.0 %)

Table 4 Surgical complications

Variable	*n* (%)
Antibiotic use	20 (5.6)
Perforation or false passage	16 (4.5)
Emergency consultation within 15 days of surgery	11 (3.1)
Endometritis	2 (0.6)
Reintervention (laparotomy)	2 (0.6)
ICU admission	2 (0.6)
Sepsis	1 (0.3)
Blood transfusion	1 (0.3)
Bowel injury	1 (0.3)
Death	1(0.3)
Bladder injury	0 (0)
Water intoxication	0 (0)

ICU intensive care unit

according to the results of clinical evaluation at the post-operative review (first few days after surgery) rather than to an institutional protocol for this purpose. Three patients experienced major transoperative complications: one had cardiorespiratory arrest on anesthesia induction, with resuscitation in the operating room and admission to the ICU, where she remained for 3 days. Another patient had uterine perforation with need for exploratory laparotomy and partial colon resection. The third major complication occurred in the patient with advanced metastatic cancer who developed abdominal sepsis after hysteroscopy. She was submitted to exploratory laparotomy and blood transfusion and died 12 days after the procedure. Complications were reported based on clinical data from the patients' medical records. No routine laboratory screening tests were performed for the diagnosis of water intoxication.

Discussion

In the present study, the prevalence of premalignant and malignant lesions (2.9 % overall, with atypical hyperplasia in 2.6 % and adenocarcinoma in 0.3 %) was within the range described in the literature (0–12.9 %) [6–10, 12, 17–19]. Previous reports show significantly higher risk of malignancy in older patients, especially after menopause [6, 7, 10–12, 14, 16, 20–22]. Again, our results are in agreement with the literature, since nine of our ten patients with malignant/premalignant lesions were postmenopausal. Only one patient was premenopausal, but also experienced abnormal bleeding. Bleeding is the most important predictor of malignancy in endometrial polyps [10, 14, 16, 19, 20, 23, 24].

We did not observe a relationship between malignancy and ultrasonographic endometrial thickness and polyp size. Similarly, there was no correlation between malignancy and comorbidities (DMand SH), BMI or use of hormone therapy. The observed increase in the frequency of malignant and premalignant lesions in patients taking tamoxifen was obvious, but not statistically significant ($p = 0.059$). Despite the association between tamoxifen use and breast cancer [25, 26], no published data are available showing a similar association with malignant polyps.

The treatment of asymptomatic polyps is controversial. Some observational studies have reported similar frequencies of malignancy in symptomatic and asymptomatic patients, favoring resection, especially after menopause [1, 6–8, 11, 21, 22, 27]. Nevertheless, based on retrospective data from all hysteroscopic polypectomy procedures performed over an 8-year period as well as on previous reports in which there was no association between asymptomatic polyps and malignancy [10, 14, 16, 18, 20, 23, 24], we question the routine surgical removal of asymptomatic polyps.

The decision to submit asymptomatic patients to surgical hysteroscopy must take into account the associated risk. The frequency of uncomplicated hysteroscopic polypectomy in our sample was 88.6 %, as previously reported [28, 29]. However, severe complications did occur in 0.9 % of the patients. These facts must be weighed against the low probability of a malignant/premalignant finding in asymptomatic patients.

In conclusion, based on the present evidence, routine indication for hysteroscopic polypectomy in asymptomatic patients is unclear. Because the natural course of endometrial polyps is still unknown, as are the factors contributing to malignancy, further prospective studies including larger numbers of patients are required to guide treatment recommendations.

Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to disclose. The authors have had full control of all primary data and they agree to allow the journal to review their data if requested. The authors have no financial relationships relevant to this article to disclose.

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