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Clinical factors and malignancy in endometrial polyps. Analysis of 1027 cases

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ABSTRACT

Study objective: To assess the prevalence of polyps carrying a malignancy and match association between clinical factors and oncologic progression.
Study design: A retrospective study (Canadian Task Force classification II-3) at a university hospital in Rome, Italy. We retrospectively analyzed data from 1027 women consecutively treated for endometrial polyps at our center in the period 2002–2011. The association of malignancy with hormonal status, tamoxifen, hypertension, symptoms, diabetes mellitus, obesity, and hormonal replacement therapy in pre- and post-menopausal women was assessed.
Results: Mean age was 45.8 ± 10.8 years. Benign polyps accounted for 95.8% of the total, pre-malignant for 2.67%, malignant for 1.54%. Our data showed that post-menopausal and older women (>60 y) with endometrial polyps have a higher risk of developing a related endometrial cancer (OR: 3.05, 95% CI [1.54, 6.19], $p < 0.001$ and OR: 2.8, 95% CI [1.38, 5.56], $p \leq 0.003$. Also we observed that women with AUB in the post-menopausal period displayed a risk of malignancy (OR: 31.1, 95% CI [10.3,111], p value <0.001).
Conclusion: Special attention should be drawn to symptomatic post-menopausal patients that appear to be at higher risk of malignancy. Symptomatic pre-menopausal women and asymptomatic post-menopausal women with polyps may be a group with intermediate-risk. These patients should undergo an individualized management plan, balancing both risks and benefits of surgical intervention after discussion with the patient.

Introduction

Endometrial polyps represent a localized overgrowth of the endometrium, projecting above the epithelium. They show a higher rate of incidence in patients between 30 and 50 years of age [1,2]. Prevalence in the normal population is about 24% (range 13–50%) and ranges from 10 to 30% in women with abnormal uterine bleeding (AUB). Incidence at autopsy is about 10% [3,4]. Presentation includes inter-menstrual or post-menopausal bleeding, infertility, persistent bleeding following curettage, or polyps may also show as an incidental finding at routine transvaginal ultrasounds. [5–7]. The use of tamoxifen has been associated with their development [8,9].

Endometrial polyps are usually benign although some may be precancerous or cancerous.

Guidelines for the management of women with endometrial polyps were introduced by the American Association of Gynecologic Laparoscopists (AAGL) in 2012 [10]. However, the authors of the guidelines stressed the absence of high-quality data supporting the pathology. This is particularly true for asymptomatic women. Their management may, therefore, be even more difficult for gynecologists, who may lack sufficient data to effectively determine the most effective form of treatment and patient care.

The objective of the present study was to determine whether clinical factors could be useful for clinicians in predicting malignant transformation in a patient with endometrial polyps.

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Materials and methods

Ethics statement

All patients gave written consent to the treatment of data for scientific purpose and publication, which have been deposited in our institutional archive. As a retrospective observational study (non interventional), it does not need ethical committee approval. This is according to the Italian laws: Ministerial Circular Letter N.6 of September 2nd 2002 from the Health Ministry published on GU N.214, September 12th 2002. Ministerial Decree N.122 of May 28th 1998 (guidelines for creation and functions of Ethical Committee). All data were analyzed anonymously.

We reviewed the clinical charts of 1027 consecutive patients treated for endometrial polyps from our archive, ranging from October 2002 to December 2011. Clinical characteristics, including age, menopausal status, arterial hypertension (defined as diastolic pressure >90 mmHg and/or systolic pressure >140 mmHg), abnormal uterine bleeding, diabetes mellitus (fasting blood glucose >126 mg/dL), hormonal replacement therapy (HRT), body mass index (BMI), and the use of tamoxifen generally and the use of tamoxifen specifically as adjuvant hormonal therapy for breast cancer, were recorded.

Women were considered post-menopausal if they reported a period of amenorrhea of at least 12 months after an age of 45 years. Abnormal uterine bleeding was defined as any vaginal bleeding in post-menopausal women or irregular vaginal bleeding in women still actively menstruating.

The diagnostic work-up of each patient included a saline infusion sono-hysterography in all cases of unclear endometrial echoes. Hysteroscopic resection was performed in most cases in an outpatient setting, using a fluid distension medium and a 5 mm diagnostic sheath (Karl Storz, Tuttingen, Germany). A "see and treat" approach was employed in an in-office setting; direct treatment and a biopsy of any lesion seen under hysteroscopic vision was conducted. Some cases needed inpatient admission. In such cases, a cervical dilatation under general anesthesia and a hysteroscopic resection using a 10 mm Storz resectoscope were performed (Karl Storz, Tuttingen, Germany).

Inclusion criteria included endometrial polyps clinically detected, i.e. visible by ultrasound or presenting with vaginal bleeding; post-menopausal ultrasound endometrial thickness >5 mm with 0.1 approximation; hysteroscopic removal of the polyp(s); and proven histological diagnosis.

Polyps were distinguished histologically as benign (atrophic, functional, or hyperplastic), premalignant, and malignant [11]. Additionally, an expert gynecological pathologist reviewed the histology.

Statistical analysis was performed using Fisher exact test to test the relationship between the mentioned clinical variables and the risk of malignancy. A p value of <.05 was considered statistically significant. Odds ratios (OR) and 95% confidence interval were calculated. All analyses were performed with MedCalc for Windows, version 12.2.1.0 (MedCalc Software, Mariakerke, Belgium) and OpenEPI (Version 2.3, May 2009).

Results

A total of 973 women from the 1027 women eligible from clinical charts with a mean age of 45.8 (±10.8) years were used to complete the study. 54 patients were excluded because they did not meet the inclusion criteria. Histological assessment of the polyps revealed that 95.78% (932 out of 973) of the women studied presented polyps benign in nature; 2.67% (26 out of 973) presented polyps with pre-malignant changes; and 1.54% (15 out of 973) presented malignant polyps. Statistical analysis also showed that pre-malignant and malignant lesions were more frequent in older women. In fact, patients older than 60 years of age accounted for 41.5% (17 out of 41 cases) of pre-malignant and malignant lesions. (Odds ratios (OR): 2.8, 95% CI [1.38, 5.56], $p = 0.003$.)

A higher distribution of benign and pre-malignant lesions was also noted in women over fifty. (Benign 43.3%, pre-malignant 35.7%). Data showed also that polyps with benign features had a higher prevalence among our premenopausal women group (66.1% of all benign polyps) despite the group with malignant lesions (61.0% of all malignant and pre-malignant polyps). This might suggest a positive correlation between the menopausal status and the risk for malignancy (OR: 3.05, 95% CI [1.54, 6.19], $p < 0.001$).

The association between malignancy and symptoms was evaluated for itself and also in relation to menopausal status.

We noted that prevalence of women with AUB was slightly higher in the malignancy group (46.3%) than in the benign group (41.2%) indicating an increased risk (OR) of malignancy, 2.26 times for women with AUB in comparison to normal population, (95% CI [1.03, 5.16], $p = 0.04$).

Table 1
Description of the study sample and clinical/demographic stratification.

	Benign *n* (%)	Polyps with malignant features *n* (%)	Total *n* (%)
Overall	932 (95.8%)	41 (4.21%)	973 (100%)
Age			
<60 Years	744 (79.8%)	17 (41.5%)	761 (78.2%)
60 Years or more	188 (20.2%)	24 (58.5%)	212 (21.8%)
Menopausal status			
Pre-menopausal	616 (66.1%)	16 (39.0%)	632 (65.0%)
Post-menopausal	316 (33.9%)	25 (61.0%)	341 (35.0%)
Diabetes mellitus			
No	900 (96.6%)	37 (90.2%)	937 (96.3%)
Yes	32 (3.43%)	4 (9.76%)	36 (3.70%)
Hypertension			
No	696 (74.7%)	25 (61.0%)	721 (74.1%)
Yes	236 (25.3%)	16 (39.0%)	252 (25.9%)
Tamoxifen use			
No	872 (93.6%)	39 (95.1%)	911 (93.6%)
Yes	60 (6.44%)	2 (4.88%)	62 (6.37%)
HRT			
No	887 (95.2%)	40 (97.6%)	927 (95.3%)
Yes	45 (4.83%)	1 (2.44%)	46 (4.73%)
BMI			
<30 kg/m^2	576 (61.8%)	25 (61.0%)	601 (61.8%)
≥30 kg/m^2	356 (38.2%)	16 (39.0%)	372 (38.2%)

Table 2
Risk increment for malignancy in correlation with clinical/demographic variables.

	Odds ratio	95% CI	*p* Value
Age over 60 years	2.8	1.38, 5.56	0.003
Post-menopausal	3.05	1.54, 6.19	<0.001
AUB	2.26	1.03, 5.16	0.04
AUB/pre-menopausal	0.99	0.323, 3.17	1
AUB/post-menopausal	31.1	10.3, 111	<0.001
Diabetes mellitus	3.04	0.742, 9.23	0.06
Hypertension	1.89	0.924, 3.75	0.067
Tamoxifen use	0.745	0.0852, 3	1
HRT	0.493	0.0119, 3.06	0.717
BMI over 30 kg/m^2	1.04	0.509, 2.05	1