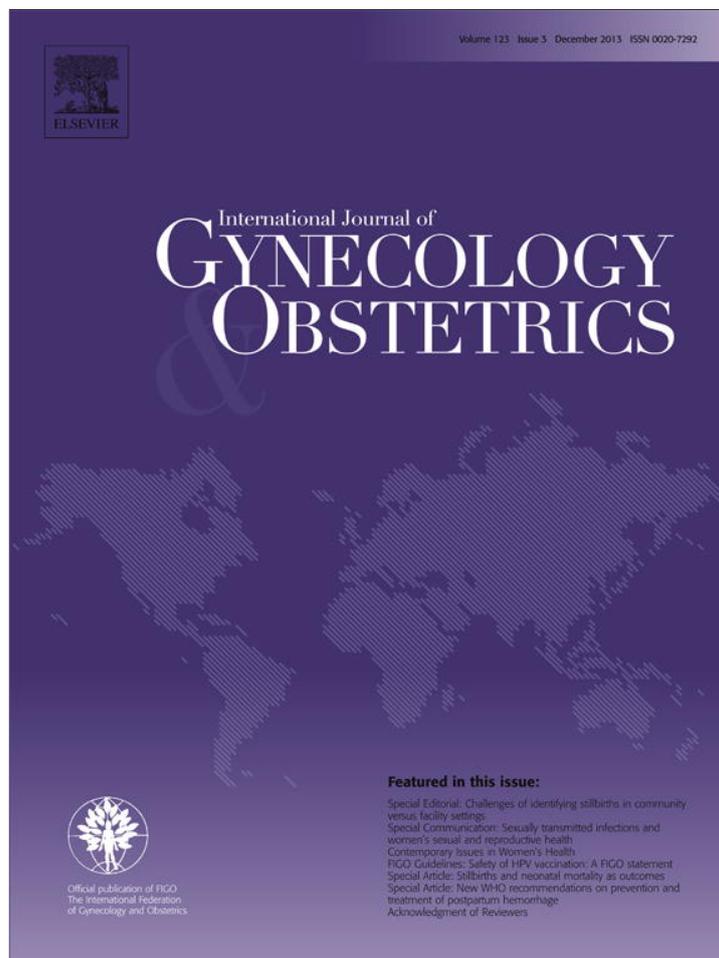


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International Journal of Gynecology and Obstetrics

journal homepage: www.elsevier.com/locate/ijgo

CLINICAL ARTICLE

Endometrial polyp size and polyp hyperplasia

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ARTICLE INFO

Article history:

Received 20 February 2013

Received in revised form 7 June 2013

Accepted 27 August 2013

Keywords:

Endometrial polyps

Hyperplasia

Hysteroscopy

Polyp sizes

ABSTRACT

Objective: To assess the correlation between the size of endometrial polyps and the histopathologic diagnosis of hyperplasia or cancer. **Methods:** A retrospective study was conducted using databases of the outpatient clinic at Antonio Pedro University Hospital in Niterói, Brazil, and of a private hysteroscopy service. The analysis included 1136 asymptomatic patients with an endometrial polyp identified on hysteroscopy, with pathologic examination, during the period 1999–2012. The polyp size, the patients' age, the indication for hysteroscopic examination, and the use of hormone medication were compared with the finding of hyperplasia in the pathologic examination. **Results:** Only polyp size showed statistical significance among the variables analyzed ($P < 0.05$). Endometrial polyps greater than 15 mm showed a hyperplasia rate of 14.8%, compared with 7.7% in the group with smaller polyps ($P < 0.05$). **Conclusion:** Endometrial polyps measuring more than 15 mm were associated with hyperplasia.

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1. Introduction

Endometrial polyp is a benign disease that affects approximately 25% of women [1,2]. It comprises stroma, glands, and vessels. It is generally asymptomatic and is diagnosed in routine exams, but it may also be related to abnormal uterine bleeding, infertility, and premalignant or malignant endometrial lesions. Endometrial polyps are present in 13–50% of women with abnormal uterine bleeding [2,3]. The origin and pathogenesis of endometrial polyps are not well known, and some factors—such as advanced age, polyp size, and associated bleeding—might be related to progression to a malignant lesion. The prevalence of malignant lesions among endometrial polyps varies from 1% to 3% [2].

The broad use of ancillary tests, such as transvaginal ultrasound, in the gynecologic workup has increased the presumptive diagnosis of endometrial polyps in asymptomatic women [1,2]. The evidence is controversial regarding treatment of these lesions [1,2,4–6].

Although hysteroscopic polypectomy is safe, there is a trend in the literature [1,5,7] to support conservative treatment (watchful waiting) for 1 year if the polyp is smaller than 15 mm and the patient is asymptomatic and has no risk factors for malignancy. This is justified by the high rate of remission of small polyps, and there is virtually no progression to malignancy in such cases [2,8].

The risk factors for malignancy are high body mass index, arterial hypertension, advanced age, postmenopausal period, and use of tamoxifen [8–10]. Hypertension and diabetes mellitus, although being considered risk factors for endometrial carcinoma, were not associated with malignant transformation of endometrial polyps in several studies [11–13]. In

a survey of 766 patients with an endometrial polyp, Wang et al. [11] identified the following risk factors for malignancy: menopausal status, size of endometrial polyps larger than 1 cm, and presence of abnormal uterine bleeding. Hypertension, diabetes mellitus, body mass index, and use of tamoxifen were not associated with the malignant transformation of polyps. In a retrospective analysis of 394 patients with endometrial polyps [12], only age emerged as a risk factor for malignancy arising in endometrial polyps after multivariate logistic regression. Diabetes and hypertension were not associated with malignant transformation; polyp size was not included in the analysis.

Transvaginal ultrasonography is a method with high sensitivity and specificity in the diagnosis of endometrial polyps. The combination with color Doppler imaging increases the diagnostic capacity of the method, enabling the identification of a single feeding vessel, which is typical of endometrial polyps [14]. Several authors [15–18] have attempted to correlate power Doppler features with the histopathologic characteristics of hyperplasia or cancer associated with endometrial polyps. However, there was no association between the pulsatility index or resistive index and histopathologic findings. Thus, the Doppler study of endometrial polyps does not replace pathology, with biopsy being mandatory in cases of suspected malignancy [18].

The objective of the present study was to assess the correlation between endometrial polyp size and histopathologic diagnosis of hyperplasia or cancer in asymptomatic patients at menopause who had a diagnosis of endometrial polyp on hysteroscopy.

2. Materials and methods

A retrospective study of asymptomatic patients at menopause (age 15–52 years) with a hysteroscopic diagnosis of endometrial polyp was conducted. The data were retrieved from databases of the outpatient

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clinic at Antonio Pedro University Hospital (Federal Fluminense University) in Niterói, Brazil, and of a private hysteroscopy service (Ginendo Clinic) in Rio de Janeiro from January 1, 1999, to December 31, 2012. The initial study database contained information on 19 795 hysteroscopies of patients aged between 15 and 98 years (Fig. 1). Patients were excluded if they were older than 52 years, had any symptoms (abdominal pain, dysmenorrhea, abnormal uterine bleeding) at presentation, had reached menopause, had colposcycytological changes, or had no endometrial polyp identified upon hysteroscopy. After exclusions, 1720 examinations were available. Of these, 491 were excluded for not containing description on polyp size, and 93 were excluded because of absent or inconclusive pathologic reports. The final analysis included 1136 hysteroscopies.

The project was approved by the Research Ethics Committee of Antonio Pedro University Hospital/Federal Fluminense University. Informed consent was not needed because the study had a retrospective design and all patients had a formal hysteroscopy indication.

Patients with infertility were not excluded from the study. Although infertility is a formal indication for polypectomy, it is not considered to be a risk factor for endometrial polyp hyperplasia. Other indications for hysteroscopy included endometritis follow-up, intrauterine device removal, endocervical polyp at speculum examination, and hysteroscopic control after myomectomy.

The data collected from each patient included age, parity, last menstrual period, indication of hysteroscopy, complaint of the patient, use of medications, imaging exam findings, and histopathology (in case of biopsies or complete excision of the lesion). The size of the endometrial polyp was defined by hysteroscopy. In case of multiple polyps, the size of the polyp submitted to biopsy was used in the analysis. All hysteroscopies were performed at the outpatient clinic, with no analgesia, using a 2.9-mm scope with a 5-FR internal sheath for the operative channel and a liquid distension medium (saline solution). All biopsies were guided (performed under direct view) using a 5-FR forceps.

To facilitate data analysis, the women were divided into groups according to age (less than 30 years, 30–40 years, and over 40 years), polyp size (up to 15 mm and greater than 15 mm), and pathologic results (hyperplastic and non-hyperplastic polyps).

The χ^2 test was used as the statistical test, with $P < 0.05$ considered to be statistically significant. The statistical software used was Stata 8.0 (StataCorp, College Station, TX, USA).

3. Results

A total of 1136 hysteroscopies were included in the study. Most patients (962 [84.7%]) were not taking hormone medication; 11 (1.0%) received tamoxifen as adjuvant treatment for breast cancer (Table 1). The disease most often associated with endometrial polyp and identified on hysteroscopy was endocervical polyp, present in 294 (25.9%) women. The main indication for undergoing hysteroscopy was an ultrasound finding of polyp or endometrial thickening ($n = 732$ [64.4%]). The mean age of the participants was 36.60 ± 6.32 years (range 21–52 years) and the mean polyp size was 12.79 ± 6.40 mm (range 1–50 mm).

Of the 1136 endometrial polyps submitted to biopsy or excision at the outpatient clinic, 102 were classified as hyperplastic upon pathologic examination. The mean size of the hyperplastic polyps was 15.05 ± 6.39 mm (range 5–35 mm), compared with 12.57 mm for the nonhyperplastic polyps. The mean age of women with a hyperplastic endometrial polyp was 40.5 ± 6.54 years (range 22–52 years). Ten (9.8%) patients received hormonal contraceptives and none received tamoxifen.

Most endometrial polyps (926 [81.5%]) measured up to 15 mm and 210 (18.5%) were greater than 15 mm. Ultrasound was the main indication for hysteroscopy in women with larger polyps (Table 2). Among the women with a polyp up to 15 mm, infertility was a common indication for the hysteroscopy, but ultrasonography was the primary

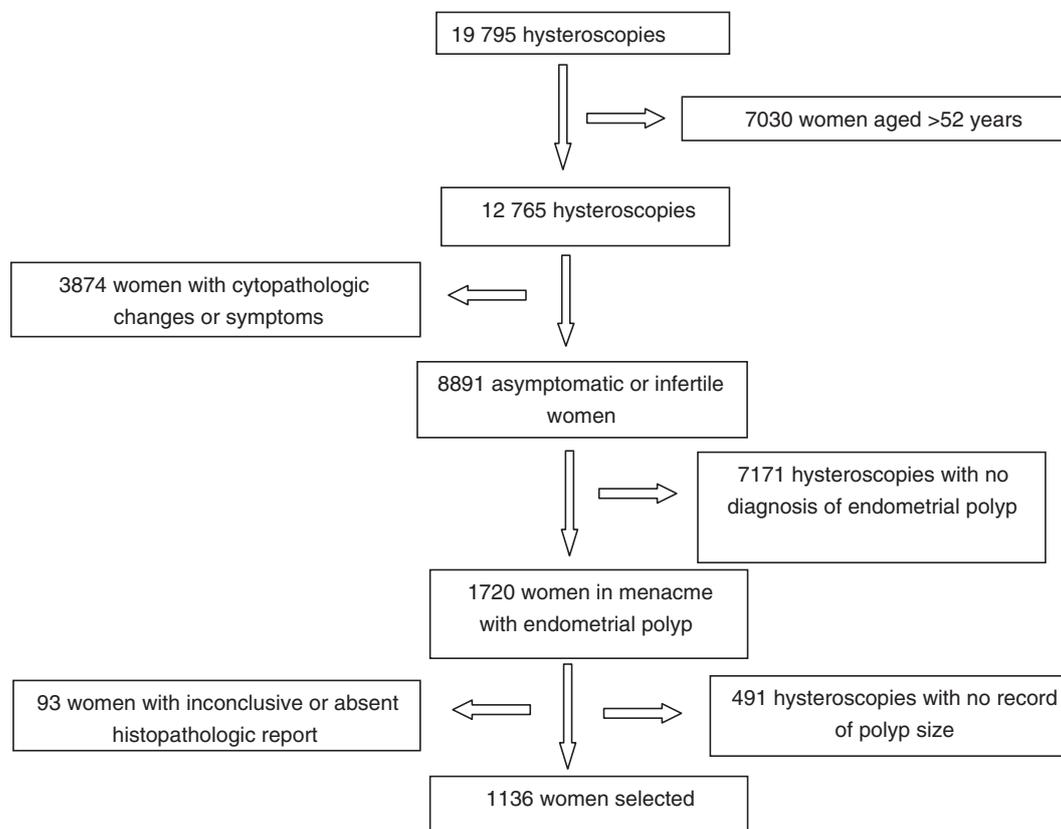


Fig. 1. Patient selection.

Table 1
Characteristics of asymptomatic patients aged up to 52 years with an endometrial polyp on hysteroscopy (n = 1136).^a

Parameter	Number (percentage)
Age, y	
<30	65 (5.7)
30–40	555 (48.9)
41–52	516 (45.4)
Parity	
Nulliparous	512 (45.1)
Up to 2 deliveries	450 (36.6)
≥3 deliveries	174 (15.3)
Abortion	
0	812 (71.5)
1	214 (18.8)
2	80 (7.1)
3	19 (1.7)
>3	11 (1.0)
Hormonal contraceptive	
Yes	174 (15.3)
No	962 (84.7)
Other associated conditions	
No conditions	661 (58.2)
Endocervical polyp	294 (25.9)
Endometrial hypertrophy	116 (10.2)
Myoma	52 (4.6)
Adenomyosis	13 (1.1)
Indication for hysteroscopy	
Ultrasound	732 (64.4)
Infertility	349 (30.7)
Other ^b	55 (4.8)
Tamoxifen	
Yes	11 (1.0)
No	1125 (99.0)

^a Values are given as number (percentage).

^b Other indications included endometritis follow-up, intrauterine device removal, endocervical polyp at speculum examination, and hysteroscopic control after myomectomy.

indication. In the group with larger polyps, the hyperplasia rate was 14.8%, compared with 7.7% in the group with smaller polyps ($P < 0.05$) (Table 3).

When the cut-off point for endometrial polyp size was changed to 10 mm, hyperplasia was found in 37 (7.2%) of the polyps up to 10 mm compared with 65 (10.4%) of the polyps greater than 10 mm. The difference was not statistically significant ($P = 0.064$).

Among the 1136 cases assessed, there was only 1 (1.0%) case of premalignant lesion (simple hyperplasia with atypia) in a 40-year-old patient using norethisterone. The size of this endometrial polyp on hysteroscopy was 10 mm.

The age of the patients showed no relation with the presence of hyperplasia in the polyp ($P > 0.05$) (Table 4).

4. Discussion

The development of an endometrial polyp can be associated with arterial hypertension, diabetes mellitus, and the presence of endocervical polyps [2,8]. In the present study, 25.9% of the patients had an associated endocervical polyp. The study did not assess the association with diabetes mellitus and hypertension because this information was not available.

Table 2
Correlation between polyp size and indication of hysteroscopy.^a

Polyp size, mm	Ultrasound	Infertility	Other	P value ^b
≤15 (n = 926)	556 (60.0)	323 (34.9)	47 (5.1)	<0.001
>15 (n = 210)	176 (83.8)	26 (12.4)	8 (3.8)	<0.001
Total (n = 1136)	732 (64.4)	349 (30.7)	55 (4.8)	–

^a Values are given as number (percentage).

^b Pearson $\chi^2 = 43.7805$.

Table 3
Correlation between polyp size and histopathology.^a

Polyp size, mm	Endometrial polyp	Hyperplastic endometrial polyp	P value ^b
≤15 (n = 926)	855 (92.3)	71 (7.7)	<0.001
>15 (n = 210)	179 (85.2)	31 (14.8)	<0.001
Total (n = 1136)	1034 (91.0)	102 (9.0)	–

^a Values are given as number (percentage).

^b Pearson $\chi^2 = 10.5423$.

The size of the endometrial polyp seems to be an important risk factor for premalignant/malignant progression of the disease. Some authors [2,19] have suggested a cut-off point of 10 mm in patients with no abnormal uterine bleeding, whereas others [9] have mentioned 15 mm. In the present series, the mean size of hyperplastic polyps was 15.05 mm, compared with 12.57 mm for the non-hyperplastic polyps. The usefulness of other tools such as Doppler ultrasonographic examination to predict the risk of malignancy has not yet been established [8,11].

The vast majority of simple hyperplasia cases occurred in polyps greater than 15 mm, corroborating previous findings [2,8–11] that conservative follow-up in patients with small asymptomatic polyps is safe. When setting the cut-off point for polyp size at 10 mm, the incidence of hyperplasia was higher in larger polyps (10.4% versus 7.2%), but the difference was not statistically significant, supporting the need for clinical follow-up of these polyps.

Although tamoxifen might be associated with the development of atypical hyperplasia [8], there was no such association in the present study. This may be explained by the small proportion of patients (1.0%) receiving tamoxifen in the sample.

There was no relation between the patients' age and the incidence of hyperplasia in endometrial polyps. This may be related to the decision to set the maximum age at 52 years. On the other hand, the main risk factor for malignancy in postmenopausal women is uterine bleeding and not age [9].

Hysteroscopic polypectomy is the gold standard method to excise endometrial polyps [19–21]. The literature corroborates conservative management for small (less than 10 mm) and asymptomatic polyps, with a high evidence level (level A) [8,19,21], the regression rate being up to 25% [2,8]. However, infertile, asymptomatic patients should undergo polypectomy to enable a better response to natural or assisted conception (level A) [19]. In symptomatic patients, polypectomy should be performed to resolve symptoms and, especially in postmenopausal women, to examine the lesion histologically [19].

At the outpatient clinic where the study took place, hysterectomy is routinely performed using a sheath with an operative channel; hence, whenever possible, biopsy or exeresis of the lesion is performed simultaneously with the diagnostic examination. Although the data indicate a different approach, we have always chosen to perform polypectomy for small polyps (less than 10 mm) with pedicles, because the lesion can be carefully removed by directing the biopsy to the lesion's base. Guided biopsy of the lesion is mandatory because even small polyps in asymptomatic women may be hyperplastic [22,23]. Office polypectomy is a secure procedure with low complication rates and should always be performed when possible, thereby avoiding further screening that would be required with a conservative approach.

Table 4
Correlation between patient age and histopathology of endometrial polyps.^a

Age, y	Endometrial polyp	Hyperplastic endometrial polyp	P value ^b
<30 (n = 65)	58 (89.2)	7 (10.8)	0.467
30–40 (n = 555)	511 (92.1)	44 (7.9)	0.430
>40 (n = 516)	465 (90.1)	51 (9.9)	0.261
Total (n = 1136)	1034 (91.0)	102 (9.0)	–

^a Values are given as number (percentage).

^b Pearson $\chi^2 = 1.5219$.

Despite the large number of patients in the present study and the fact that biopsies were guided to areas of major changes in the polyp, the results might have been influenced by the use of biopsies rather than whole lesions for the pathologic examination.

Further studies, preferably with a prospective design, should be carried out to evaluate the prevalence of premalignant/malignant lesions in asymptomatic postmenopausal patients. It should also be assessed whether the vascular pattern of the polyp and the condition of the endometrium (thickness, irregularity) are associated with the risk of hyperplasia.

According to the present study, it is safe to perform watchful waiting in asymptomatic women in menopause with an endometrial polyp smaller than 15 mm, as corroborated by the literature [2,19,24,25]. Endometrial polyps greater than 15 mm were associated with a higher rate of hyperplasia.

Conflict of interest

The authors have no conflicts of interest.

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