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## Analysis of 1,469 outpatient hysteroscopies performed in a Brazilian hospital

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### ABSTRACT

**Objective.** To evaluate medical records of patients who underwent outpatient hysteroscopy at the Mario Covas State Hospital between 2017 and 2022, correlating findings with the anatomopathological results and clinical features.

**Materials and Methods.** Cross-sectional observational study. All data were collected in a standardized form based on medical record data of a previously performed diagnostic hysteroscopy. The participants' examination date, clinical, gynaecological, and obstetric data, and data from the hysteroscopy were recorded.

**Results.** Data were collected from 1,469 women, with a mean age of  $52.6 \pm 12.65$  years and a mean BMI of  $29.14 \pm 5.32$  kg/m<sup>2</sup>. Among the patients, 499 (33.97%) had chronic hypertension and 170 (11.57%) had type 2 diabetes mellitus. Among the reasons for requesting the examination, cases of postmenopausal endometrial thickening were the most frequent (30.50%). A correlation was identified between the presence of hyperplasia without atypia and the BMI value ( $p = 0.031$ ), as well as the presence of endometrial polyps and patients with chronic arterial hypertension ( $p < 0.001$ ), which was not identified for diabetes ( $p = 0.338$ ). Finally, there was also a correlation between cases of postmenopausal bleeding and pathological positivity for malignancy ( $p < 0.001$ ). The age of the patients was considered a risk factor for both endometrial polyps and the presence or absence of malignancy ( $p < 0.0001$  and  $p = 0.044$ , respectively).

**Conclusions.** The findings of this study reveal that adiposity correlates with endometrial hyperplasia without atypia. Similarly, hypertension and age correlate with endometrial polyps and postmenopausal bleeding, whereas age correlates with endometrial cancer.

### INTRODUCTION

In the era of minimally invasive gynaecologic surgery [1-3], hysteroscopy has helped change the management of intrauterine pathology, and pa-

tients who previously had to be hospitalized and undergone curettage or even hysterectomy for diagnosis in inconclusive cases can now undergo surgery with direct visualization of the cavity, without the need for hospitalization, anaesthesia,

or even major surgery [4,5]. In addition to being effective, this type of procedure brings safety to patients, with low complication rates such as perforations or bleeding [6]. The outpatient procedure can be used in several investigations, such as women with post-menopausal bleeding, or for investigating abnormal uterine bleeding [7] or infertility due for example submucous myomas [8-10]. Moreover, in the specific case of myomas, hysteroscopic treatment of them may be essential in preparation for pregnancy to prevent their growth and compromise pregnancy outcomes [11]. It can also complement the diagnosis of uterine synechiae, uterine malformations, ectopic pregnancies and pregnancy complications [12-17]. Compared to ultrasound, hysteroscopy has an advantage as far as accuracy is concerned, considering that approximately 20% of patients with normal ultrasound may have some hysteroscopic alteration [18]. Hospital complexes with access to hysteroscopy have a high number of patients seen every day, with the possibility of a large-scale assessment of the prevalence of uterine pathologies in the public evaluated. In 2022, for example, Patrizi *et al.* evaluated 1,020 patients who underwent surgical hysteroscopy after undergoing outpatient hysteroscopy and ultrasonography [19]. Both men- and postmenopausal women were analysed in the study, and the health characteristics of this study population contribute for the creation of health policies. In Brazil, large-scale studies assessing the prevalence of uterine polyps and the significance of endometrial abnormalities in predicting malignant and pre-malignant lesions are still scarce, and there are no national data in this regard indicating the size of our sample. Therefore, the importance of evaluating the data of the Brazilian population concerning the findings of outpatient hysteroscopy is evident, as it makes it possible to determine the prevalence of uterine pathologies, the number of patients who undergo the examination unnecessarily as well as require anaesthesia due to pain or some types of stenosis, and the number of biopsies performed that were positive for malignancy. In addition, it allows for the association of comorbidities with uterine diseases, complementing what is already known in the literature on the subject [20]. By better understanding this sample, it is possible to improve and optimize care management regarding which women would effectively need to undergo surgical interventions and which can maintain a clinical follow-up.

### **Purpose**

The main objective of this study is to analyse the medical records of patients who underwent outpatient hysteroscopy at the Centro Universitário Faculdade de Medicina do ABC between the years 2017 and 2022. The secondary objective of this study is to evaluate the prevalence of intrauterine pathologies, correlating them with anatomopathological findings and comorbidities.

### **MATERIALS AND METHODS**

A cross-sectional study was conducted by investigators who were members of the Gynecologic Endoscopy Department of the Centro Universitário Faculdade de Medicina do ABC. All data were collected on a standardized form based on medical record data from diagnostic hysteroscopy previously performed.

Patients who underwent diagnostic hysteroscopy at the Mário Covas State Hospital in Santo André, Brazil, between May 2017 and December 2022 were invited to participate. Those interested were included after a detailed explanation and signing the informed consent form. It is important to emphasize that they were referred to the hospital after having initially undergone a medical consultation, either at the hospital itself or at a primary care service in the State of São Paulo, when the need for the procedure in question was verified. Outpatient hysteroscopies were performed using the same type of diagnostic jacket system with a working channel with a 4.3 mm inner sheath, with a 5 Fr channel for semi-rigid instruments, a 5 mm outer sheath, a Hopkins system with a 30-degree viewing angle of 2.9 mm and 30 cm in length with the possible use of mechanical tools (biopsy forceps, alligator and 5 Fr scissors) or a 16 Fr bipolar mini resectoscope. All specimens removed from the cavity are routinely sent for anatomopathological study at the pathology laboratory of Centro Universitário Faculdade de Medicina do ABC. All procedures were performed by multiple surgeons, including trainees or staff of the hysteroscopy sector of the FMABC university centre.

### **Standardized outpatient hysteroscopy form**

The patients' examination date and clinical data were recorded. Patients with a body mass index

equal to or greater than 25 kg/m<sup>2</sup> and less than 30 kg/m<sup>2</sup> were considered overweight, and patients with a body mass index equal to or greater than 30 kg/m<sup>2</sup> were considered obese [21]. The woman was considered with the diagnosis of hypertension considering the blood pressure measurement on two different days, with the systolic pressure readings on both days of ≥140 mmHg and/or the diastolic pressure readings on both days of ≥ 90 mmHg [22].

Concerning the patient’s obstetric history, the number of pregnancies the woman had, as well as the number of deliveries and abortions, the date of the last menstruation, the age at which she entered menopause, and the reason for the examination, such as the presence of postmenopausal bleeding, abnormal uterine bleeding or if she was referred for alteration of any examination only, among others, were recorded. In addition, a record was made of whether the patient had used hormone replacement therapy, with its respective details, whether the patient used any contraceptive method, with the description of the method, if any, whether an intrauterine device was inserted or removed, whether the woman had a reproductive desire, or whether she suffered from abnormal uterine bleeding.

Regarding the hysteroscopy, the indication for the examination, previous ultrasound examination, and whether it was performed with sedation were initially analysed. Regarding the endocervical canal, information was recorded on whether dilatation was necessary, whether the cervix’s external

orifice was patent, and the endocervical canal and the internal orifice of the cervix. In case any endocervical polyp was identified, the number, size, whether it was pedunculated or sessile, how it was vascularized, and location in the cervix were noted. The size and shape of the endometrial cavity, the type of endometrium identified, the characteristics of the isthmus, and the presence of polyps were recorded, with the same descriptions used for cervical polyps. The presence of synechiae, uterine malformations, and fibroids was also recorded, with a description of size, topography, base extension, penetration, and if they affected the lateral wall, with the Lasmar score [23]. The study analysed whether a biopsy was performed in the case, with a description of how this biopsy was performed and whether a new hysteroscopy or surgical hysteroscopy was indicated, correlating the anatomopathological finding identified from the biopsy. This study included all patients who met the selection criteria (convenience sample) for the stipulated analysis time, with an expected sample size of approximately one thousand participants. Participants’ characteristics were presented descriptively (minimum, maximum, numbers, percentages, median, and standard deviation).

Data were distributed using the Kolmogorov-Smirnov test. Chi square, Fisher’s or Student’s t-tests were used according to the nature of the variables. When data had non-normal distribution, non-parametric tests were used. P-values < 0.05 were considered statistically significant. The missing data were classified as an individualized

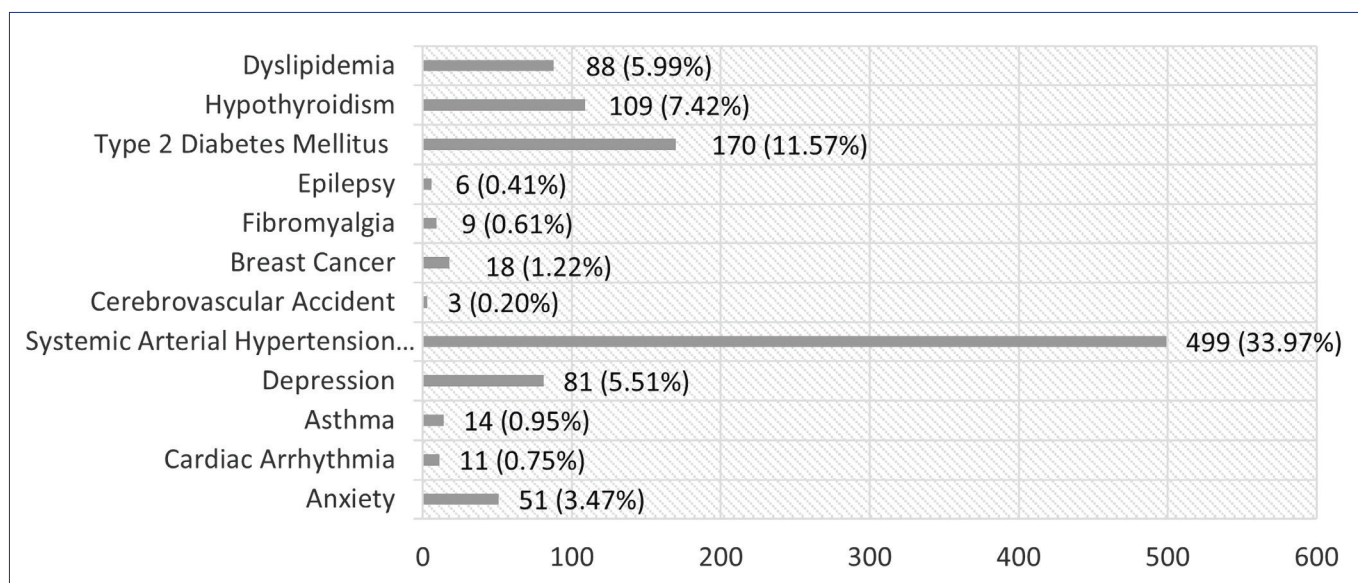


Figure 1. Classification of the population according to associated comorbidities.

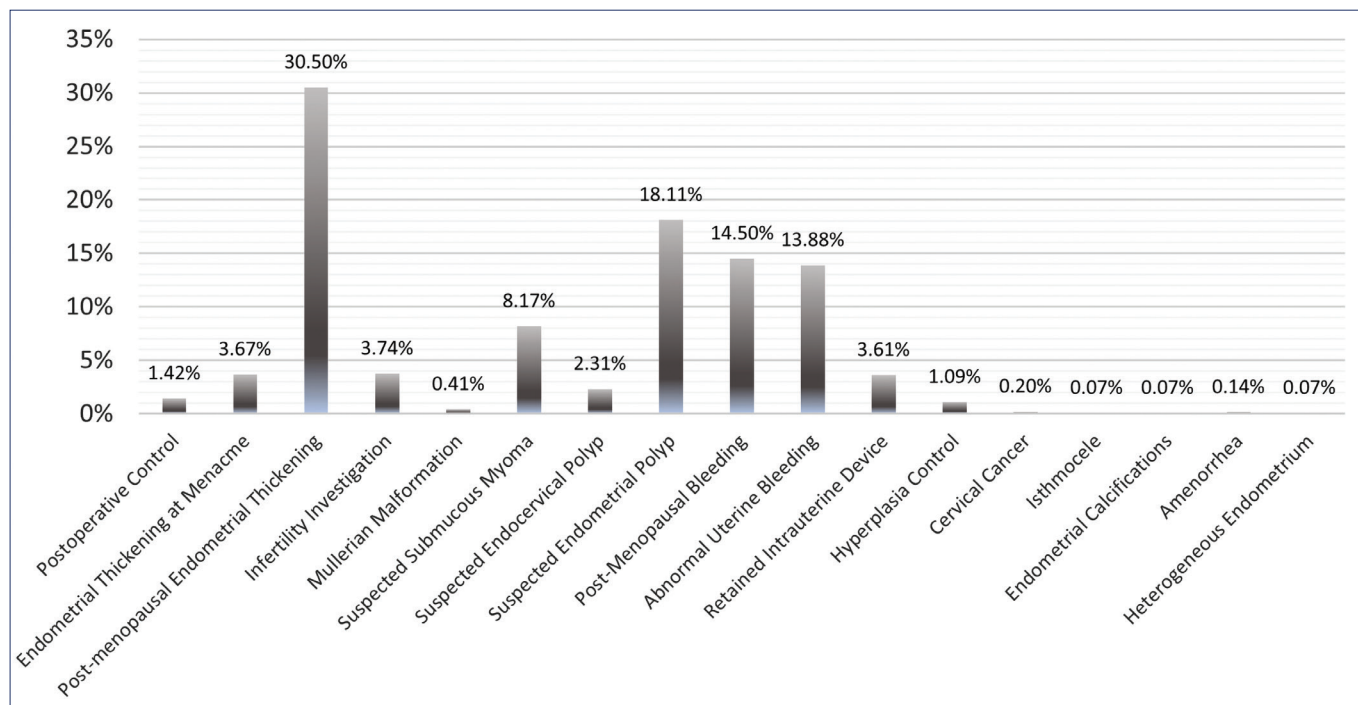


Figure 2. Analysis of the reasons for referral for hysteroscopy.

category among the answers so that there were no interferences within the statistical correlation.

The data obtained were organized in electronic spreadsheets of the Microsoft Excel® 2018 software version 1910 (Microsoft Corporal®, San Diego USA).

Female patients over 18 years of age who passed an evaluation with the hysteroscopy sector, who their procedure performed between May 2017 and December 2022, and who agreed to participate in the study, were included. Pregnant patients, women with suspected active intrauterine infection or active uterine bleeding on admission were excluded.

Patients weighing more than 100 kg were also excluded due to the maximum capacity of the examination stretcher.

### RESULTS

Data were collected from 1,469 women, with a mean age of 52.6 ± 12.65 years and a mean body mass index (BMI) of 29.14 ± 5.32 kg/m<sup>2</sup>. The frequency of obese patients was 29.47%, with grade 1 being the most frequent (64.43%). In addition, 390 overweight patients were evaluated (26.55% of the total).

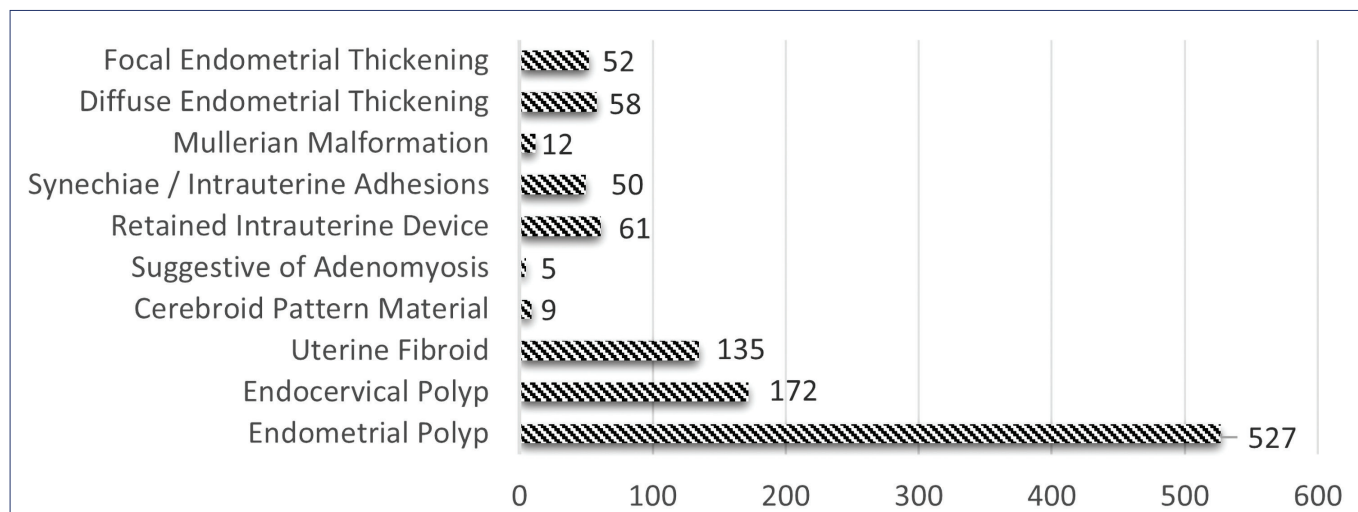


Figure 3. Uterine abnormalities described in hysteroscopies.

Among the patients (**Figure 1**), 499 (33.97%) had chronic arterial hypertension and 170 (11.57%) had type 2 diabetes mellitus.

Only 3.67% of the records described analgesia with sedation, and in 7.35% of the cases the procedure had to be interrupted due to pain, 5.78% due to severe stenosis of the external orifice of the cervix, and 10.48% due to stenosis of the internal orifice.

Among the reasons for requesting the examination (**Figure 2**), cases of post-menopausal endometrial thickening were the most frequent, with 448 cases (30.50%). The patients were referred for suspicion of endometrial polyp in 18.11% of the medical records and for suspicion of endocervical polyp in 2.31%.

The abnormal hysteroscopic findings are described in **Figure 3**. In 527 (35.87%) of the cases, the presence of endometrial polyps inside the uterine cavity was identified. The second most common finding was endocervical polyps (11.70%), followed by intrauterine fibroids (9.19%).

A total of 323 biopsies were performed, and the pathology results were located in 72.75% of the cases since the virtual results system was introduced in the hospital only in 2018. Among the results, 48.51% had a positive anatomopathological result for polyps (endometrial or endocervical), and 5.96% were diagnosed with some endometrial hyperplasia. In 31.06% of the cases, the biopsy result was without indication of abnormalities, and in 3.83% of the anatomopathological studies, the sample was considered insufficient for analysis. In the analysis of the samples, 7.66% had a positive result for malignancy. Considering the biopsied endometrial polyps with available reports, the malignancy rate was 3.60%. Statistical analysis showed a correlation between post-menopausal bleeding and positive pathology for malignancy ( $p < 0.001$ ). It should be noted that 83.3% of patients diagnosed with cancer had this symptom. Regarding clinical features, a statistically significant correlation was identified between hyperplasia without atypia and BMI ( $p$

**Table 1.** The frequency of endometrial polyps and anatomopathologic positivity for malignancy at hysteroscopy according to clinical characteristics and endometrial thickness.

Parameter Assessed	M (± dp)	Endometrial polyps at hysteroscopy M (± dp)	P-value	Pathology showing malignancy M (± dp)	P-value	
Age	52.59 ± 12.65	55.87 ± 11,14	< 0.001	63.89 ± 8.17	0.044	
IMC (kg/m <sup>2</sup> )	29.14 ± 5.32	29.29 ± 5.43	0.418	29.08 ± 6.44	< 0.001	
	<b>n (%)</b>	<b>n (%)</b>	<b>P-value</b>	<b>n (%)</b>	<b>P-value</b>	
Post-menopausal women	Yes	793 (53.98)	350 (44.13)	< 0.001	17 (2.14%)	< 0.001
No	676 (46.02)	177 (26.18)	1 (0.14%)			
Chronic hypertension	Yes	499 (33.97)	216 (43.28)	< 0.001	9 (1.80)	< 0.001
No	970 (66.03)	311 (32.06)	9 (0.93)			
Type 2 diabetes mellitus	Yes	170 (11.57)	67 (39.41)	0.34	4 (2.35)	5.55
No	1299 (88.43)	460 (35.41)	14 (1.08)			
Use of tamoxifen	Yes	27 (1.84)	11 (40.74)	0.54	0 (0)	0.28
No	1442 (98.16)	516 (35.78)	18 (1.24)			
Hormone therapy	Yes	14 (0.95)	0	1.14	0 (0)	1.14
No	1455 (99.05)	9(0.2)	9 (0.62)			
Obesity	Yes	433 (29.47)	156 (36.03)	0.48	7 (1.62)	< 0.001
No	1036 (70.53)	227 (21.91)	7 (0.67)			
<b>Endometrial thickness in postmenopause</b>						
> 4 ≤ 10 mm	174 (11.84)	74 (42.53)	0.374	1 (0.57)	0.035	
> 10 ≤ 16 mm	53 (3.61)	28 (52.83)	0.598	1 (1.89)	0.072	
> 16 mm	22 (1.50)	12 (54.54)	0.577	2 (9.09)	0.027	

= 0.031). As shown in **Table 1**, an association was also identified between the presence of endometrial polyps and the existence or not of chronic hypertension ( $p < 0.001$ ), which did not occur when the comorbidity studied was type 2 diabetes mellitus ( $p = 0.338$ ). Obesity, present in 29.47% of patients, was not shown to be a clinical risk factor for the development of endometrial polyps ( $p = 0.48$ ). On the other hand, obese patients had a positive correlation with positive pathology for malignancy. The patients' age and post-menopausal status were associated with both endometrial polyps and the presence or absence of malignancy ( $p < 0.0001$  and  $p = 0.044$ , respectively). The presence of endometrial polyps was higher in the group of patients with endometrial thickness above 10 mm (around 54.54%) compared to women with endometrial thickness between 4 and 10 mm (42.53%). Statistical analysis showed a statistical correlation between cases of endometrial thickness above between 4 and 10 mm and the probability of pathology showing malignancy or not, as well as cases of thickening above 16 mm.

## DISCUSSION

Outpatient hysteroscopies are responsible for the diagnosis of several uterine abnormalities, being a highly resolutive procedure. In the study, approximately 1,081 abnormal intrauterine macroscopic findings were located among the 1,469 patients evaluated. Despite the significant number of reports analysed, a malignancy rate of only 7.66% was observed among the biopsies. The malignancy rate among endometrial polyps, which was 3.60%, was similar to that found in other studies, indicating an estimated malignancy prevalence between 3.4 and 4.9% for post-menopausal women [24, 25]. Future studies should investigate the correlation between endometrial and/or cervical polyps and malignant lesions, perhaps investigating the presence of an altered vaginal microbiome or the concomitant presence of ovarian lesions [26, 27]. According to a systematic review by Uglietti *et al.*, published in 2019, which found a prevalence of malignant polyps of 2.73% (95%CI 2.57-2.91), there is a very high heterogeneity among studies focused on this subject [28].

Chronic arterial hypertension was the most frequent comorbidity among the patients evaluated, evidencing itself as a clinical risk factor for

the presence of endometrial polyps. On the other hand, type 2 diabetes mellitus, the second most frequent disease, did not show the exact correlation. The link between endometrial polyps and clinical conditions is uncertain in the literature. Some data suggest, for example, that obesity, hypertension, and diabetes mellitus may promote endometrial thickening and uterine diseases through the release of growth factors such as IGF-1, which would increase the risk of developing endometrial polyps [29-31]. If the figure really correlated, it would make sense to undertake appropriate strategies to prevent type two diabetes mellitus through improved glucose compensation [32]. Because polyps are extremely common in pre-menopausal women, their correlation with diabetes would also worsen reproductive outcomes, so a call to action would be necessary at that point [33-35].

Studies, such as that of Serhat *et al.* [36] and Al-sannan *et al.* [37], point to obesity as a risk factor for endometrial polyps. In contrast, hypertension and diabetes mellitus do not have the same relationship [36, 37]. It is worth mentioning that the prevalence of such underlying diseases tends to increase with age and postmenopausal status, which may interfere with data analysis, also observed in this study [38]. Although obesity was not characterized as a comorbidity associated with the presence of endometrial polyps, a statistical correlation was identified between BMI and the presence or absence of such polyps. This disagreement may have occurred since the group analysed had a high frequency of overweight patients. In addition, obesity was statistically correlated with endometrial hyperplasia without atypia. Such an association is noteworthy, especially because BMI may be a risk factor for occult atypical hyperplasia, as portrayed according to the study by Hui *et al.*, Etrusco *et al.* and Garuti *et al.* [39-41].

Among the reasons for referral for hysteroscopy, the cases of postmenopausal bleeding, present in 14.5% of cases, were noteworthy and showed to be a clinical risk factor for malignancy. This finding is in line with the data of Ferrazzi *et al.*, for example, who showed a tenfold increase in the risk of endometrial cancer among patients who had vaginal bleeding compared to asymptomatic women [42]. The number of referrals for endometrial thickening, involving postmenopausal patients or not, also drew attention. It should be emphasized that there is no cut-off number for

estimating menopausal women with endometrial thickening, considering there is intense variability within the menstrual cycle. In general, the literature recommends individualization of cases, and endometrial biopsy is appropriate, mainly in cases where there is associated abnormal uterine bleeding [43]. In the case of postmenopausal women, according to the American College of Obstetricians and Gynecologists (ACOG), cases of thickened endometrium are considered when the endometrial echo value exceeds 4 mm for women without the use of hormone replacement therapy [44, 46]. Our study showed an increase in the frequency of endometrial polyps accompanying the increase in endometrial thickness in postmenopausal women, especially after 10 mm of thickness. A statistical correlation with malignancy was also identified in some cases.

The rate of hysteroscopy interruption due to pain or cervical stenosis varies in the literature. According to Coimbra AC *et al.* for example, tolerance was considered terrible or poor in 14,9% of hysteroscopies, with low tolerance associated to menopause and lack of previous vaginal delivery [47]. These patients were more likely to benefit from pain relief measures during office hysteroscopy. The study identified 7.35% stoppage of the examination due to pain complaints of the patient and 16.26% due to stenosis of the cervix. It is noted that some factors may contribute to the sensation of pain in the procedure, such as the fact that it is a teaching hospital, in which many of the examinations are performed by residents. According to a study by Pegoraro *et al.* conducted with 489 patients, for example, a statistical correlation was identified between the visual analogue scale and the surgeon's experience [48]. Also contributing to this rate of interruption of the examination may have been the fact that many procedures are performed with a diagnostic shirt only instead of a Bettocchi System, which could overpass the problems of the cervical stenosis assessed.

Among the weaknesses of this study is that it was cross-sectional, with a single interaction with the patients. Among the strengths, we highlight the large number of participants with varying ages. It is emphasized that the data of this study cannot be generalized to the entire population because it is a cross-sectional study, conducted in patients selected through a convenience sample. The result may also have been influenced by the intense racial miscegenation in the Brazilian population.

## CONCLUSIONS

Our study demonstrates that there is a correlation between BMI and endometrial hyperplasia without atypia. There was also an association between the presence of endometrial polyps and chronic arterial hypertension and a relationship between post-menopausal bleeding, obesity and BMI, and positive pathology for malignancy. Finally, there was a statistical correlation between endometrial thickening above 4 mm and the finding of endometrial polyps and endometrial cancer.

## COMPLIANCE WITH ETHICAL STANDARDS

### *Authors' contribution*

M.M.S.: Writing – original draft, formal analysis. T.M.: Conceptualization, supervision. F.V., A.A., G.N.A.: Data curation. M.T., C.E.F.: Writing – review & editing, supervision.

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### *Study registration*

N/A.

### *Disclosure of interests*

The authors declare that they have no conflict interests.

### *Ethical approval*

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Centro Universitário Faculdade de Medicina do ABC (Date 08/29/2022 /CAAE No 60645522.7.0000.0082).

### *Informed consent*

Informed consent was obtained from all individual participants included in the study.

### *Data sharing*

Data are available under reasonable request to the corresponding author.

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