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Histological assessment of endometrial polyps resected by hysteroscopy

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Abstract. – OBJECTIVE: This study aimed to analyze the clinical data and pathologic aspects of endometrial polyps (EMPs) excised completely during surgical hysteroscopy and assess the connection between premalignant and malignant EMPs.

PATIENTS AND METHODS: This retrospective study includes 489 participants who underwent hysteroscopy due to endometrial polyps, and the clinical features and histological findings of the resected polyps analyzed.

RESULTS: Participants with EMPs were divided into six groups according to histologic findings. The histologic finding of most cases was simple benign endometrial polyp [397 patients (81.2%)]. Malignant polyp was detected in 3 patients (0.6%). The histologic findings according to age, menopausal status, and menstrual bleeding patterns at the time of presentation to the outpatient clinic were compared; however, no significant difference was observed. 237 patients were observed to have menometrorrhagia, which was the most prevalent symptom reported. The distribution of polyp sizes observed at hysteroscopy according to histologic findings was compared, but no significant difference was observed.

CONCLUSIONS: EMPs are often benign but can include premalignant or malignant tissue changes. Hysteroscopy is used for direct observation of the uterine cervix and resection of existing polyps, considering the increasing frequency of its use as a diagnostic and treatment tool.

Key Words:
Endometrial polyps, Histological findings, Hysteroscopy, Saline infusion sonography.

Introduction

Endometrial polyps (EMPs) are a gynecological condition linked to abnormal uterine bleeding, bleeding between periods, infertility, and potentially cancerous disorders. They are prevalent during the premenopausal or postmenopausal years. Patients may be asymptomatic, and gynecologists may diagnose them incidentally during pelvic imaging, cervical cytology, endometrial biopsy results, or physical examination[1]. Gynecologists may possibly identify them while assessing female infertility[2].

EMPs are hyperplastic overgrowths of endometrial glands, which can be single or multiple, measuring from a few millimeters to centimeters, sessile or pedunculated, extending from endometrial intrauterine cavities[2,3]. Most polyps arise from the fundal region and extend to the internal os. Occasionally, they project through the external cervical os and can be seen in the vagina. They can be single or several, a few millimeters to a few centimeters in size, and attached or not[2,3].

EMPs were 7.6% in premenopausal women and 13% in postmenopausal women[4]. EMP prevalence is higher in infertile women (6-30%), suggesting they contribute to infertility[5]. The incidence of this complication is 5% or greater in patients who undergo endometrial biopsy or hysterectomy, ranging from 10 to 24%[5,6]. Additional risk factors for EMPs comprise age, obesity, tamoxifen use, hormone replacement treatment, and Lynch and Cowden syndrome. Although most EMPs are harmless, they have the potential to become hyperplastic, with malignant transformation occurring in 0.7% to 12.9% of polyps in documented case series[7]. The risk is elevated if the individual is postmenopausal and experiencing symptoms. Various molecular mechanisms have been suggested to contribute to the formation of endometrial polyps, such as monoclonal endometrial hyperplasia[8], increased expression of endometrial aromatase[9,10], somatic gene mutations[11,12], and age-related buildup of low-frequency single nucleotide variants in oncogenes like

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Kirsten Rat Sarcoma Viral Oncogene homolog (KRAS), Phosphatase and Tensin homolog deleted on chromosome ten (PTEN) and Tumor Protein (TP53).

In 64-88% of EMP patients, abnormal vaginal bleeding is the main symptom. Intermenstrual bleeding is the most prevalent type of premenopausal EMP bleeding. Small amounts of bleeding may occur as spotting. Symptoms are unrelated to polyp number, size, or location[13]. Polyps are present in 21% to 28% of women experiencing postmenopausal hemorrhage[14-16].

Transvaginal ultrasonography (TVUS) is the preferred initial imaging method for assessing patients with abnormal bleeding or suspected uterine polyp[17]. On TVUS, EMP is usually seen as a bright lesion with smooth margins within the uterus and surrounded by a narrow, bright halo[18].

A saline infusion sonogram (SIS) and diagnostic hysteroscopy are utilized to assess patients with an EMP and postmenopausal patients with a thickened endometrium on TVUS[19]. They improve the sonographic contrast of the endometrial cavity, enabling precise determination of the size, location, and other features of the EMP. Using SIS, polyps are shown as echogenic, smooth, intracavitary masses with distinct outlines created by fluid, either at their broad bases or slender stalks. SIS can detect small EMPs that may not be identified by gray-scale TVUS, which could enhance diagnostic precision[20,21]. Unlike hysteroscopy, SIS can examine the uterine cavity, pelvic tissues, and myometrial and adnexal defects. SIS has a higher learning curve than non-contrast TVUS, a difficult time diagnosing endometrial disease, and balloon catheter fluid leaks or pain[22].

Hysteroscopy is considered the most reliable method for diagnosing endometrial polyps[23]. A hysteroscopy is a type of telescope used to examine the endometrial cavity, tubal ostia, endocervical canal, cervix, and vagina by inserting it through the vagina and cervix into the uterus. Hysteroscopy can be done for either diagnostic or therapeutic purposes. Hysteroscopy's primary benefit is the capacity to both observe and eliminate polyps at the same time. Diagnostic hysteroscopy provides a subjective evaluation of the lesion's size, position, and physical traits. It has a sensitivity ranging from 58% to 99%, specificity from 87% to 100%, positive predictive value from 21% to 100%, and negative predictive value from 66% to 99% compared to hysteroscopy with guided biopsy[24-26]. Although office hysteroscopy is becoming more common, most regular diagnostic hysteroscopies are still done in an operating room with anesthesia and hospital stay[27-29]. Flexible hysteroscopy is comfortable and easier to navigate through the cervical canal than rigid[29,30], making it appropriate for outpatient treatments. This approach has 74% poorer sensitivity than rigid hysteroscopy for endometrial polyp detection[31-34].

Contraindications for hysteroscopy include intrauterine pregnancy, pyometra, active pelvic infection (including genital herpes infection), and diagnosed cervical malignancy[35-37]. Although rare, complications from hysteroscopy can be life-threatening[38-41]. The primary complication is uterine perforation, with other complications, such as fluid overload, intraoperative hemorrhage, bladder or bowel damage, and endometritis. Embolism, whether air or carbon dioxide, can happen with any hysteroscopic procedure and may lead to cardiovascular collapse[41]. Radiofrequency or laser light can cause thermal damage to the uterine cavity, intestine, urinary bladder, and major pelvic arteries[41]. The likelihood of infection following surgical hysteroscopy is minimal. We aimed to examine the clinical data and histological characteristics of completely excised endometrial polyps during surgical hysteroscopy and assess parameters associated with premalignant and malignant variations.

Patients and Methods

This retrospective study was conducted at the Umraniye Training and Research Hospital in Istanbul, Turkey. The data obtained from the medical records of 514 women in our center between 2015-2017 were retrospectively analyzed, and the clinical features and histological diagnoses of the resected polyps were evaluated. Twenty-five patients were excluded from the study because of insufficient data in the file. In addition, seventy-two patients underwent operative hysteroscopy, but no polyps were found, resection was not performed, and histopathology was not evaluated, so they were excluded from the study. In three postmenopausal patients, uterine perforation was observed, and they were excluded from the study. Patients who presented to the gynecology outpatient clinic with abnormal uterine bleeding (AUB) and underwent operative hysteroscopy because of suspicion of endometrial polyps because of TVUS or SIS, polyp resection, and histopathology evaluation were included in the study. The TVUS examination was performed using a 5

mHz vaginal probe and was performed at any time of the menstrual cycle. Endometrial line (EL) assessment was performed by evaluating both layers in both longitudinal and transverse directions, covering the internal space from the os to the fundus, aiming for a straight, regular, well-defined border. As a criterion for suspicion of EMPs, there is a hyperechoic lesion with regular contours within the uterine lumen. Some of the patients with suspected EMPs underwent SIS, and the others underwent direct hysteroscopy.

We conducted SIS on premenopausal women during the early follicular phase of the menstrual cycle, post-menstruation, and before day 10 when the endometrium is at its thinnest. Anesthesia is not required as an intrauterine insemination catheter was used. The catheter was inserted into the fundus with a ring forceps through the cervical os. The speculum was withdrawn cautiously to prevent displacing the catheter. A vaginal probe was inserted, and a syringe containing saline was connected to the catheter. Saline was gradually infused into the cavity. If polypoid lesions were present in the cavity, hypoechoic, heterogeneous intracavitary masses were observed. No side effects related to this procedure were observed in any patient.

Patients in whom we planned hysteroscopy because of TVUS, SIS, or clinical suspicion of EMPs were first informed about the success and complications of the procedure. We conducted hysteroscopy on premenopausal women with a regular menstrual cycle during the proliferative phase, as it is the best time for optimal viewing of the uterine cavity. We gave 200 mcg of misoprostol vaginally to individuals expected to require cervical dilatation 24 hours before the surgery. The antibiotics for prophylaxis were not administered. All patients undergoing operative hysteroscopy were anesthetized, then placed in the lithotomy position, and a sterile field was established. We inserted the hysteroscope into the cervical os, observed the uterine cavity, and removed the observed polyps using a resectoscope. We chose the distention medium 5% mannitol. Fluid overload, a very serious complication of hysteroscopy, was never observed in our patients. In 3 postmenopausal patients, uterine perforation was observed, and the procedure was canceled. No other complications were observed.

Statistical Analysis

Research data were presented as numbers (percentage) and medians (min-max). The nominal data of volunteers divided into subgroups according to histologic diagnosis were compared using Chi-square and Kruskal-Wallis ANOVA with a Mann-Whitney test for post-hoc comparisons. Analyses were performed with SPSS for Windows version 26 software (IBM Corp., Armonk, NY, USA). A *p*-value lower than 0.05 was significant.

Results

The office hysteroscopic polypectomy was successfully performed in all 489 patients. The histopathologic diagnoses of them are given in Table I. The histopathologic result of most cases was endometrial polyp [397 patients (81.2%)]. Adenomyomatosis was found in 4 patients (0.08%) and leiomyomas in 39 cases (8.0%). In 18 patients (3.7%), the presence of endocervical polyps was reported. Hyperplasia was detected in 10 patients (2.0%) with atypia and in 15 patients (3.1%) without atypia in a polyp. We found histologically uncommon results categorized as 'Others' from six patients (2.2%). In Table II, the histopathologic diagnoses of the endometrial polyp cases that we reported as 'Others' are described.

In Table III, we divided the cases histologically into benign, premalignant, and malignant. Simple EP, EP with adenomyomatosis, leiomyoma, endocervical polyp, and 3 histopathologic diagnoses in the 'Others' list formed the benign category. Hyperplasia with and without atypia was considered premalignant, and 25 patients were diagnosed as premalignant. Endometrial polyp and mesenchymal tumors with high malignant potential, which are included in 'Others' in Table II, were considered malignant. Endometrioid carcinoma (grade I) and mixed-type adenocarcinoma (endometroid, serous carcinoma) (grade III) were the other malignant histopathologic diagnoses. Malignant polyp was detected in a total of 3 patients (0.6%).

Table I. Histopathologic diagnosis of endometrial polyps resected at operative hysteroscopy.

Diagnosis	Count (%)
Simple EP	397 (81.2%)
EP with adenomyomatosis	4 (0.08%)
EP without atypical hyperplasia	15 (3.1%)
EP with atypical hyperplasia	10 (2.0%)
Simple endocervical polyp	18 (3.7%)
EP with leiomyoma	39 (8.0%)
Others	6 (1.2%)
Total	489 (100%)

EP: Endometrial polyp.

Table II. Histopathologic diagnosis of endometrial polyps reported as in the category of "Others".

Diagnosis	Count (%)
Tubal metaplasia on endocervical polyp	1 (0.2%)
Endometrial polyp with mesenchymal tumor with high malignant potential	1 (0.2%)
Endometrial polyp with mesenchymal lesion with diffuse hyalinized oval-spindle cell morphology	1 (0.2%)
Inflamed, necrotic decidua, sparsely degenerated necrotic chorionic villi (resting placenta?)	1 (0.2%)
Endometrioid carcinoma developed on polypoid, diffuse atypia endometrial hyperplasia, FIGO grade: I/III	1 (0.2%)
Mixed-type adenocarcinoma on endometrial polyp 80% endometroid, 15-20% serous carcinoma, histologic grade (endometrioid carcinoma): III/III, nuclear grade: III/III	1 (0.2%)

FIGO: International Federation of Gynecology and Obstetrics.

Table IV shows the classification of histopathologic results according to age, gravida, parity, mode of delivery, menopausal status, and menstrual bleeding patterns at the time of presentation to the outpatient clinic. However, no significant difference was observed in any of them. The median value of EMPs with atypical endometrial hyperplasia (EH) was 56 (36-73) years – it was not significant but higher than others. Also, the 2nd highest age group was the 'Others' group [46 (34-67)], which includes 3 malignant histopathologic diagnoses. Except for endometrial polyp (EP) with atypical hyperplasia, most of the other cases were observed in the premenopausal period. Although not significant, 6 of 10 patients with EP with atypical hyperplasia were observed in the postmenopausal period. Menometrorrhagia was the most common symptom observed in all cases [237 patients (48%)].

The distribution of histopathologic diagnoses according to the ultrasonographic findings examined beforehand is shown in Table V. Although it was not statistically significant, leiomyoma was diagnosed at a higher rate on histopathologic examination in patients in whom leiomyoma was detected on TVUS. The distribution of polyp sizes observed at hysteroscopy according to histopathologic results is shown in Table VI. Multiple polyps were the most common in all groups, although not significantly.

Table III. Differentiation of histopathologic diagnoses as benign, premalignant and malignant endometrial polyps.

Diagnosis	Count (%)
Benign	461 (94.3%)
Premalignant	25 (5.1%)
Malign	3 (0.6%)
Total	489 (100%)

Discussion

A total of 489 cases of endometrial polyps underwent hysteroscopy. In our study, we found the rate of premalignant and malignant lesions to be 5.7%. This rate was slightly higher compared to other studies[42,43], probably because we considered hyperplasia without atypia as premalignant. Savelli et al[42] reported the frequency of carcinoma in endometrial polyps as 0.8%, hyperplasia with atypia at 3.1%, and hyperplasia without atypia at 25.7%. In another study by Ben-Arie et al[43], 3.3% of atypical hyperplasia and 3.0% of endometrial adenocarcinoma were detected. We found that the frequency of carcinoma in endometrial polyps was 0.6%, hyperplasia with atypia was 2.0 %, and hyperplasia without atypia was reported as 3.1%. Our rates were lower in carcinoma in endometrial polyps.

In this study, two of the patients with endometrial cancer were premenopausal, and one was postmenopausal. The common feature of all three patients was the complaint of vaginal bleeding at the outpatient clinic. In similar studies, patients with endometrial cancer were mostly in the postmenopausal period[44,45], while in our study, it was found to be premenopausal.

A study[46] found that the prevalence of endometrial polyps was strongly affected by age ($p<0.005$). In women under 30 years old, the frequency was 0.9%. Polyps were seen in 5.8% of premenopausal women and 11.8% of postmenopausal women, with a statistically significant difference ($p<0.01$)[45]. The average age in our study was above 40 years. Surprisingly, the percentage of premenopausal women was larger than that of postmenopausal women, with 78.7% and 21.3%, respectively, which differs from prior studies.

Hemorrhaging is the predominant first symptom, seen in 64 to 88 percent of individuals with polyps[46,47]. The predominant symptom in our

Table IV. Distribution of histopathological diagnoses according to clinical factors and types of abnormal uterine bleeding.

	Simple EP (n=397; 81.2%)	EP with adenomyomatosis (n=4; 0.08%)	EP without atypical EH (n=15; 3.1%)	EP with atypical EH (n=10; 2.0%)	Simple endocervical polyp (n=18; 3.7%)	EP with leiomyoma (n=39; 8.0%)	Others (n=6; 1.2%)	*p*
Age	42 (18-78)	41.5 (31-54)	45 (28-65)	56 (36-73)	44.5 (23-70)	43 (20-72)	46 (34-67)	NS
Gravida	3 (0-13)	2.5 (0-5)	4 (0-10)	4 (1-8)	2 (0-7)	3 (0-15)	4 (0-13)	NS
Parity	2 (0-12)	2 (0-4)	3 (0-4)	3.5 (1-7)	2 (0-7)	2 (0-12)	3 (0-4)	NS
NSD	2 (0-12)	1.5 (0-2)	3 (0-4)	3.5 (0-7)	2 (0-7)	2 (0-12)	3 (0-4)	NS
C/S	0 (0-4)	0 (0-3)	0 (0-3)	0 (0-1)	0 (0-1)	0 (0-3)	0 (0-1)	NS
Premenopause								
Yes	318 (80.3%)	3 (75%)	12 (80%)	4 (40%)	13 (72.2%)	30 (76.9%)	5 (83.3%)	NS
No	78 (19.7%)	1 (25%)	3 (20%)	6 (60%)	5 (27.8 %)	9 (23.1%)	1 (16.7%)	
Postmenopause								
Yes	76 (19.1%)	1 (25%)	2 (13.3%)	6 (60%)	5 (27.8%)	9 (23.1%)	1 (16.7%)	NS
No	321 (80.9%)	3 (75%)	13 (86.7%)	4 (40%)	13 (72%)	30 (76.9%)	5 (83.3%)	
Postmenopausal hemorrhage								
Yes	35 (8.8%)	1 (25%)	2 (13.3%)	2 (20%)	3 (16.7%)	4 (10.3%)	1 (16.7%)	NS
No	362 (91.2%)	3 (75%)	13 (86.7%)	8 (80%)	15 (83.3%)	35 (89.7%)	5 (83.3%)	
Hypermenorrhagia								
Yes	165 (41.6%)	1 (25%)	7 (46.7%)	4 (40%)	6 (33.3%)	14 (35.9%)	3 (50%)	NS
No	232 (58.4%)	3 (75%)	8 (53.3%)	6 (60%)	12 (66.7%)	25 (64.1%)	3 (50%)	
Menometrorrhagia								
Yes	194 (48.9%)	1 (25%)	8 (53.3%)	3 (30%)	10 (55.6%)	17 (43.6%)	4 (66.7%)	NS
No	203 (51.1%)	3 (75%)	7 (46.7%)	7 (70%)	8 (44.4%)	22 (56.4%)	2 (33.3%)	
Oligomenorrhagia								
Yes	5 (1.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	NS
No	392 (98.7%)	4 (100%)	15 (100%)	10 (100%)	18 (100%)	39 (100%)	6 (100%)	

EP: Endometrial polyp; EH: Endometrial hyperplasia; NSD: Normal spontaneous delivery; C/S: Caesarean Section; NS: Not significant.

Table V. Distribution of histopathologic diagnoses according to ultrasonographic findings.

	Simple EP (n=397; 81.2%)	EP with adenomyomatosis (n=4; 0.08%)	EP without atypical EH (n=15; 3.1%)	EP with atypical EH (n=10; 2.0%)	Simple endocervical polyp (n=18; 3.7%)	EP with leiomyoma (n=39; 8.0%)	Others (n=6; 1.2%)	*p*
Leiomyoma								
Yes	33 (8.3%)	0 (0%)	1 (6.7%)	1 (10%)	2 (11.1%)	8 (20.5%)	0 (0%)	NS
No	363 (91.7%)	4 (100%)	14 (93.3%)	9 (90%)	16 (88.9%)	31 (79.5%)	6 (100%)	
Leioyoma diameter (mm)	28 (10-58)				14.5 (10-19)	21 (9-38)		NS
Endometrial polyp observed saline infusion sonography								
Yes	96 (75.8%)	1 (25%)	2 (13.3%)	0	5 (27.8%)	7 (17.9%)	2 (33.3%)	NS
No	301 (24.2%)	3 (75%)	13 (86.7%)	10 (100%)	13 (72.2%)	32 (82.1%)	4 (66.7%)	
Endometrial polyp observed Saline infusion sonography (mm)	14 (4-45)	18.5 (7-30)			15 (10-20)	12 (8-25)	10.5 (5-16)	NS
Endometrial line (mm)	10 (4-35)	10 (7-13)	10 (5-24)	11 (8-27)	10 (7-23)	10 (4-25)	10 (7-19)	NS
Endometrial polyp observed on ultrasonography								
Yes	157 (39.5%)	1 (25%)	5 (33.3%)	1 (10%)	5 (27.8%)	16 (41%)	3 (50%)	NS
No	240 (60.5%)	3 (75%)	10 (66.7%)	9 (90%)	13 (72.2%)	59 (59%)	3 (50%)	
Endometrial polyp observed on ultrasonography (diameter, mm)	12 (4-80)		14 (8-18)		10 (6-19)	12.5 (7-24)	7 (7-35)	NS

EP: Endometrial polyp; EH: Endometrial hyperplasia; NS: Not significant.

Table VI. Distribution of histopathologic diagnoses according to polyp size observed at hysteroscopy.

	Simple EP (n=397; 81.2%)	EP with adenomyomatosis (n=4; 0.08%)	EP without atypical EH (n=15; 3.1%)	EP with atypical EH (n=10; 2.0%)	Simple endocervical polyp (n=18; 3.7%)	EP with leiomyoma (n=39; 8.0%)	Others (n=6; 1.2%)	*p*
Polyp observed in hysteroscopy (diameter, mm)								
1. Multiple polyp	220 (55%)	3 (75%)	13 (86.7%)	10 (100%)	10 (55.6%)	17 (43.6%)	3 (50%)	NS
2. ≤10 mm	96 (24.2%)	1 (25%)	1 (6.7%)	0 (0%)	3 (16.7%)	9 (23.1%)	1 (16.7%)	
3. 11-20 mm	51 (12.9%)	0 (0%)	0 (0%)	0 (0%)	4 (22.2%)	11 (28.2%)	2 (33.3%)	
4. >20 mm	29 (7.3%)	0 (0%)	1 (6.7%)	0 (0%)	1 (5.6%)	2 (5.1%)	0 (0%)	

EP: Endometrial polyp; EH: Endometrial hyperplasia; NS: Not significant.

study was bleeding, with 237 patients experiencing menometrorrhagia and 200 patients experiencing hypermenorrhea.

Information on the relationship between polyp size and the likelihood of developing cancer is not well-defined. The study found no significant difference in polyp size between hysteroscopy and histopathologic data. Consequently, the polyp size was not associated with malignancy or premalignancy. The meta-analysis evaluation found contradictory results on whether larger polyp size was linked to malignancy[48]. A later meta-analysis[49] found no association between polyp size (≥2 and <2 cm) and malignancy.

No significant difference was detected between endometrial lining thickness measured by transvaginal ultrasound (TVUS) and histopathologic outcomes in this investigation. Out of 200 postmenopausal females with bleeding, a thicker endometrium (>4 mm), and a negative endometrial biopsy in a randomized study[19], two patients had undetected endometrial cancer, and one patient had endometrial hyperplasia with atypia in polyps.

Limitations of the Study

This study's weaknesses include the lack of homogeneity across the six groups based on histologic findings. The small sample size in the study groups impeded the statistical examination of specific data.

The limited size of the sample prevented reaching statistical significance, even though there were differences in specific factors.

Conclusions

Overall, EMPs are often harmless, although they can include tissue changes that may lead to cancer. Hysteroscopy is increasingly utilized to directly visualize the uterine cavity and endometrium to diagnose and remove polyps. Hysteroscopic polypectomy is effective and dependable for both diagnosis and treatment. Hysteroscopy enables quick recovery, a prompt return to normal activities, and a brief hospital or office visit.

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Ethics Approval

This study was approved by the Local Ethics Committee of the Umraniye Training and Research Hospital, Ethical Committee for Scientific Research and Publications (Registry No.: 68; Dated March 5, 2020). The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments.

Informed Consent

Written informed consent could not be obtained from the patients included in the study due to the study's retrospective design and voluntary participation.

Conflict of Interest

The authors have disclosed that they have no significant relationships with, or financial interest in, any other commercial companies pertaining to this article.

Authors' Contributions

ST, ES: study concept, data collection, editing; ST, AO: analysis, writing; AO, AC: literature review, editing; ST, CB: study concept, analysis, data checking, editing.

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