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Malignancy Risk of Endometrial Polyps Among Geriatric Women

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SUMMARY

Background: The population of elderly women is increasing worldwide. Here we investigated the prevalence of malignant endometrial polyps in a population of geriatric women. Methods: This retrospective study was conducted at the gynaecology clinic of Zekai Tahir Burak Education and Research Hospital. Women who were aged >65 years and who were pathologically diagnosed with endometrial polyps between 2007 and 2016 were included. All patients with endometrial polyps underwent hysteroscopic resection. Patient characteristics, complaints and imaging and surgical findings were obtained from their medical records. Statistical data analysis was performed using SPSS software. Results: In total, 133 geriatric female patients were included. They had a mean age of 68.96 ± 4.20 (65 -83) years. Among them, 114 (85.7%) patients had benign endometrial polyps, 7 (5.2%) had endometrial hyperplasia and 12 (9%) had endometrial cancer. Forty-eight women had been admitted because of postmenopausal bleeding. Eighty-five women presented with either non-specific symptoms, such as abdominal pain, dysuria and urinary incontinence, or had no symptoms and received incidental diagnosis via ultrasound scanning. The mean endometrial thickness was 9.3 ± 6.39 mm in benign cases and 16.44 + 8.64 mm in premalignant/malignant cases. In multivariate Cox regression analysis, uterine bleeding and endometrial thickness were significantly and independently associated with premalignant or malignant polyps.All malignant polyps were found to be endometrioid adenocarcinoma.

Conclusion: In our study, we detected an prevalence of endometrial cancer among 9% of geriatric women with endometrial polyps. Hence, it is important to conduct a pathological evaluation of endometrial polyps in such patients.

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1. Introduction

An endometrial polyp is defined as a localised overgrowth of the endometrium that may contain glands, fibrous tissue and blood vessels in variable amounts.^{1,2} These gynaecological lesions are common and are estimated to affect up to 20% of postmenopausal women.^{1,3,4} Although endometrial polyps are usually asymptomatic, they are also a common cause of abnormal uterine bleeding in both pre- and postmenopausal women.³ Endometrial polyps are usually benign; however, they have been found to be associated with carcinogenesis and hyperplasia in approximately 0.8%–12.9% of patients.^{5–7} Several risk factors, including obesity, age, hypertension, hormone replacement therapy, polycystic ovary syndrome (PCOS) and tamoxifen use, have been identified.^{8–10}

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The increased use of transvaginal ultrasonography and in-office hysteroscopy during the past 20 years has led to an increase in the detection of asymptomatic polyps.¹¹ A few percent of malignant cases among patients with endometrial polyps has been reported; however, postmenopausal women with polyps have an increased risk of malignancy compared with pre-menopausal women with polyps.¹² Although a pathologic examination is necessary for a definitive diagnosis, follow-up treatment can also be chosen for some postmenopausal patients.¹³

The aim of this retrospective study was to evaluate the prevalence and predictors of premalignant and malignant polyps in a population of geriatric women.

2. Methods

In this retrospective study, we reviewed the medical records of 133 women aged \geq 65 years who had been diagnosed with



Original Article





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endometrial polyps and had undergone hysteroscopic polypectomy at the gynaecologic clinic of the Zekai Tahir Burak Women's Health Education and Research Hospital between January 2007 and December 2016. This study was approved by the local ethics committee (no: 01.27.2016/13), All patients provided an informed consent regarding research use of their medical information.

Through a retrospective review of medical records, we obtained patient characteristics such as age, body mass index (BMI), years elapsed since menopause, history of hormone or tamoxifen therapy, history of systemic hypertension (HT) and diabetes mellitus (DM) and ultrasonographic findings.

Systemic HT was defined as diastolic and systolic blood pressure >90 mmHg and ≥140 mmHg, respectively. In addition, women taking antihypertensive drugs were considered hypertensive. Those who were previously diagnosed with DM and were under treatment or who had a fasting plasma glucose level >110 mg/dL were considered as having DM. All women underwent transvaginal ultrasonography followed by a complete pelvic examination. Women with suspicious ultrasound findings, such as endometrial thickening, underwent in-office hysteroscopy. All in-office procedures were performed on an outpatient basis without anaesthesia. In-office hysteroscopy was performed using a 5-mm continuousflow mechanical office hysteroscope with 30° rod lens (Karl Storz, Tuttlingen, Germany). All women diagnosed with polyps underwent operative hysteroscopy under general anaesthesia. Distention of the uterine cavity was achieved using 1.5% glycine solution. Hysteroscopic resection was performed with a monopolar cutting loop and a 10-mm rigid resectoscope. Microscopic specimens were assessed by our pathology department.

Statistical analyses were performed using the Statistical Package for the Social Sciences, version 21.0 (SPSS, Inc., Chicago, IL, USA). Normal distribution of the data was assessed using the Kolmogorov–Smirnov test. Continuous and normally distributed variables were presented as mean \pm standard deviation, and intergroup differences were evaluated using the Student's *t*-test. Continuous variables with non-normal distribution were expressed as medians (minimum–maximum), and differences between variables were analysed using the Mann–Whitney *U* test. Differences with respect to categorical data were evaluated using the chi-square test. Receiver operating characteristic analysis of the area under the curve was used to identify discriminative parameters between the groups. Binary logistic regression analysis was used to reveal risk factors for endometrial polyps. A P value of <0.05 was considered to indicate statistical significance.

3. Results

We analysed the data of 133 patients who underwent hysteroscopic polypectomy. The baseline characteristics of the patients are presented in Table 1. All patients were postmenopausal and were aged >65 years, with a median age of 68 years (range, 65–83 years). Approximately 29.3% of patients had DM and 42.1% had HT. Vaginal bleeding was reported in 36.1% of patients.

Table 2 shows the histological diagnosis of the resected endometrial polyps. In most cases, benign endometrial polyps (85.7%) were detected. Premalignant lesions comprised one polyp (0.8%) with simple hyperplasia with atypia and six polyps (4.5%) with complex hyperplasia with atypia. Twelve malignant polyps (9%) were detected.

Univariate analysis of the factors associated with the risk of malignancy is shown in Table 3. Both endometrial thickness and uterine bleeding were found to be significantly associated with abnormal histology. In the multivariate Cox regression analysis, uterine bleeding and endometrial thickness were found to be

Table 1

Baseline characteristics of women with endometrial polyps (n = 133).

| | Ν | % |
|------------------------------------|----|-------|
| Age (years) | | |
| \leq 70 | 95 | 71.4 |
| >70 | 38 | 28.6 |
| Vaginal bleeding | 48 | 36.1 |
| Use of hormone replacement therapy | 7 | 5.3 |
| Diabetes mellitus | 39 | 29.3 |
| Hypertension | 56 | 42.1 |
| BMI (kg/m ²) | | |
| <18.5 | 0 | 0% |
| 18.5–24.9 | 6 | 4.5% |
| 24.9-29.9 | 35 | 26.5% |
| >30 | 92 | 69% |

Table 2

Histological diagnosis of endometrial polyps resected during hysteroscopy.

| Histological Diagnosis | Ν | % |
|--|-------------------|------|
| Benign | 114 | 85.7 |
| Endometrial polyp | 107 | 80.5 |
| Polyp with no atypia/simple hyperplasia | 4 | 3 |
| Polyp with no atypia/complex hyperplasia | 3 | 2.3 |
| Premalignant/Malignant | nant/Malignant 19 | |
| Polyp with atypia/simple hyperplasia | 1 | 0.8 |
| Polyp with atypia/complex hyperplasia | 6 | 4.5 |
| Endometrial carcinoma | 12 | 9 |

significantly and independently associated with premalignant or malignant polyps (Table 3).

4. Discussion

Cancers, especially gynaecologic malignancies, are considered as diseases of elderly women. Approximately 47% of all cancer cases in the USA occur in patients aged 65–84 years.¹² Some studies conducted on various age groups have found that while menopause itself is a risk factor for endometrial cancer, the rate of malignancy increases among women aged >60 years.^{13–18} In this study, we observed an prevalence of malignant polyps in 9% of the cases in a cohort of 133 patients with polyps aged >65 years. However, when all age groups are considered, the risk of endometrial cancer for women with endometrial polyps is 4.8%.^{5,14} A study by Hileeto et al¹⁸ identified endometrial malignancies in 32% of 115 women with endometrial polyps aged >65 years, whereas a study by Lee et al¹² identified malignancies in 3.1% of 159 women with polyps aged >65 years. Previous studies have also reported atypical hyperplasias in biopsies in 0.3%–3.3% of women with endometrial polyps.^{5,14} Similarly, in our study, the prevalence of atypical hyperplasia was 5.3% in patients aged >65 years. We attribute these inter-study differences to the use of several diagnostic procedures and the inclusion of various study groups.

Geriatric women do not generally undergo regular gynaecologic examinations unless they have complaints. One of the most frequent complaints at the time of presentation is vaginal bleeding. Postmenopausal bleeding has been identified as a possible risk factor for malignancy of endometrial polyp.¹⁷ In a study by Ferrazi, postmenopausal patients with vaginal bleeding were found to have a 10-fold greater risk of cancer compared with asymptomatic patients.¹³ In another study by Machtinger et al, both age and presence of vaginal bleeding were found to be associated with cancer.¹⁹ Consistent with these studies, we observed a significantly higher prevalence of uterine bleeding in premalignant/malignant cases vs. benign cases (79% vs. 29%). In our multivariate analysis, we identified uterine bleeding as a significant indicator of malignancy

Table 3

Univariate analysis of demographic and clinical factors in patients with normal and abnormal histological outcomes.

| Variable | Univariate Analysis | | | Multivariate Analysis | | |
|---------------------------|----------------------------------|--|---------|-----------------------|-------------|---------|
| | Benign Polyp Group ($n = 114$) | Premalignant/Malignant Polyp Group (n = 19) | P Value | OR | 95% CI | P Value |
| Age, years | 68 (65-83) | 67 (65–81) | NS | | | |
| Parity | 3 (0-9) | 3 (0-9) | NS | | | |
| BMI | 32.33 ± 5.4 | 33.84 ± 4.44 | NS | | | |
| Hypertension | 48 | 8 | NS | | | |
| Diabetes mellitus | 34 | 8 | NS | | | |
| Polyp median diameter, cm | 2.39 ± 0.98 | 1.89 ± 1.04 | NS | | | |
| Endometrial thickness, mm | 9.3 + 6.39 | 16.44 + 8.64 | <0.001 | 0.24 | 0.71-0.83 | <0.025 |
| Uterine bleeding | | | <0.001 | 0.13 | 0.04 - 0.45 | <0.001 |

Abbreviations: NS, not significant.

of endometrial polyp in a population of geriatric women (odds ratio, 0.13; 95% confidence interval, 0.04–0.45). Asymptomatic geriatric patients with identified endometrial thickening should receive the same management as symptomatic patients, including endometrial biopsy.⁵ In our study, 21% of the patients identified with malignancy were asymptomatic.

Although previously published studies have focussed on the correlation between the size of the polyp and malignancy, a full consensus has not yet been reached. A study by Hassa et al found no correlation between symptomatology and the number, localisation and size of polyps.²⁰ Fernandez et al found that the risk of endometrial cancer increased with increasing polyp size.²¹ In contrast, Ferrazi et al found that the risk of endometrial cancer increased only in polyps of size >18 mm.¹³ Ben-Arie et al also found that malignancy increased with increasing polyp size.¹⁴ However, we did not identify any association between the polyp size and malignancy. Although endometrial adenocarcinoma most frequently accompanied endometrial polyps in our study cohort, previous studies have most frequently identified the same serous type in elderly women with polyps.

Lee et al conducted a meta-analysis in which obesity was found to increase the risk of malignancy in endometrial polyps.¹² Bergman et al observed that patients who used tamoxifen demonstrated a higher incidence of endometrial polyps and those diagnosed with endometrial cancer had a more aggressive histological type and grade ²². In our study, we evaluated BMI, presence of DM and HT and history of tamoxifen use among the potential accompanying risk factors; however, we were unable to find any significant differences between patients with benign and malignant lesions with respect to these risk factors.

In conclusion, no consensus has been reached regarding the management of endometrial polyps diagnosed in geriatric women. Our study findings indicate the importance of further evaluation of suspected endometrial polyps in women after gynaecological and ultrasonographic examination.

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