Assessment of Endometrial Sampling and Histopathological Results: Analysis of 4,247 Cases

Endometrial Örnekleme ve Histopatoloji Sonuçlarının Değerlendirilmesi; 4.247 Olgunun Analizi

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ABSTRACT

Objective: This study aimed to investigate the relationship between indications and histopathological results in patients undergoing endometrial sampling.

Materials and Methods: Data of 4,247 patients undergoing endometrial sampling due to non-obstetric gynecological causes between January 2010 and October 2016 were retrospectively evaluated using the archives of the Gynecology and Obstetrics Clinic of Konya Training and Research Hospital.

Results: The mean age of patients was 46.8 ± 8.22 years; the most common indication was menometrorrhagia/menorrhagia (70.66%), and the least common indication was cervical polyp (1.34%). The most common histopathological result was proliferative-secretory endometrium (63.62%); simple hyperplasia with atypia (0.56%) was determined to be the least common result. Endometrial cancer was observed more frequently in the post-menopausal bleeding and increased endometrial thickness group (23.11%). Of patients in whom biopsy was performed, 52.18% had undergone hysterectomy, as a result of which proliferative–secretory endometrium was most commonly (59.52%) and simple hyperplasia with atypia least commonly found as the histopathological diagnosis.

Conclusion: Although sampling should be performed following endometrial evaluation in patients with post-menopausal bleeding or increased endometrial thickness, according to the results of our study, routine endometrial biopsy should not be preferred in the other indications.

Keywords: Endometrial sampling, endometrial cancer, hysterectomy, histopathological examination

ÖZ

Amaç: Bu çalışmada kliniğimizde endometrial örnekleme yapılan olgularda endikasyonlar ile histopatolojik sonuçlar arasındaki ilişkinin araştırılması amaçlanmıştır.

Gereç ve Yöntem: Kliniğimizde Ocak 2010 - Ekim 2016 yılları arasında başvuran ve obstetrik dışı jinekolojik endikasyonlar nedeni ile endometrial örnekleme yapılan 4,247 olgunun verileri Kadın Hastalıkları ve Doğum Kliniği ve Patoloji Kliniği arşiv kayıtlarından retrospektif olarak taranarak değerlendirildi.

Bulgular: Olguların yaş ortalaması 46,8+8,22 olup en sık endikasyon menometroraji-menoraji (%70,66) iken en az servikal polip (%1,34) idi. Endometriyal biyopsi sonucu proliferatif-sekretuar endometriyum (%63,62) en sık atipili basit hiperplazi (%1,13) en az histopatolojik sonuç olarak tespit edildi. Endometriyum kanseri postmenaposal kanama ya da endometriyal kalınlık grubunda daha fazla oranda gözlendi (%23,11). Biyopsi yapılan olguların %52,18%'ne histerektomi ameliyatı yapılmıştı. Histerektomi sonucu proliferatif-sekretuar endometriyum (%59,52) en sık atipili basit hiperplazi (%1,13) en az histopatolojik sonuç olarak tespit edildi.

Sonuç: Postmenapozal kanama ya da endometrial kalınlık artışı olan olgularda endometriyal değerlendirmeyi takiben örnekleme yapılması uygunken, çalışmamız sonuçlarına göre diğer endikasyonlarda rutin olarak endometrial biyopsi tercih edilmemelidir.

Anahtar Kelimeler: Endometriyal örnekleme, endometriyum kanseri, histerektomi, histopatolojik inceleme

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Introduction

Abnormal uterine bleeding is among the most common causes of admissions to gynecology clinics, and it is of great importance as it is the most common sign of anemia in the pre-menopausal period and suspicion of malignancy in the post-menopausal period. Endometrial sampling is recommended for patients under 35 years of age with ovulatory bleeding or for patients above 35 years of age with abnormal bleeding [1, 2]. Endometrial sampling, which is widely used for the diagnosis and treatment of endometrial pathologies, is performed using dilation curettage (D/C), aspiration (office biopsy), and hysteroscopy methods [3]. Use of D/C, which was first described by Recaimer

in 1843 and was widely used, is now used less commonly due to its requirement of anesthesia, high morbidity, perforation risk, and high cost [1, 3]. Currently, sampling methods such as Pipelle, which is easier, inexpensive, and can be used under office conditions are preferred [4]. D/C and office biopsy methods enable the complete evaluation of the endometrium as only one-third of the endometrium can be evaluated with these methods [5]. Hysteroscopy is accepted as the gold standard for evaluating endometrial pathologies as the endometrial cavity may be directly observed with hysteroscopy, which also enables concurrent treatment [3, 6]. Recent studies report that routine endometrial sampling is controversial as they are associated with high costly, high morbidity, and anxiety in patients [5-7].

In this study, we aimed to evaluate the relationship between the indications for endometrial sampling and histopathological results in cases between January 2010 and October 2016.

Materials and Methods

After approval was obtained from the Konya Education and Research Hospital Planning and Coordinating Committee (2016-11-06), endometrial biopsy results of 4,247 patients who had undergone endometrial sampling due to gynecological causes between January 2010 and October 2016 were retrospectively evaluated. Written informed consent was obtained from all patients. Evacuation curettage patients who had undergone this procedure due to obstetrical indications such as elective pregnancy termination and pregnancy complications were excluded from the study. Data were obtained from electronic patient records and the Medical Pathology Department archives. Tissues obtained with endometrial sampling were sent to the pathology laboratory in 10% neutral formalin solution.

The indications for endometrial sampling were classified as menometrorrhagia/menorrhagia, myoma uteri, post-menopausal bleeding or an increase in post-menopausal endometrial thickness (≥5 mm), cervical polyp, and adnexal mass lesion. The histopathological results were classified as proliferative-secretory endometrium, simple hyperplasia without atypia, complex hyperplasia without atypia, simple hyperplasia with atypia, complex hyperplasia with atypia, endometrial polyp, endometritis, endometrial adenocarcinoma, atrophic endometrium, and insufficient material.

Statistical analysis

The Statistical Package for Social Sciences version 15.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analyses. The Kolmogorov-Smirnov analysis was used to assess the normality distribution of continuous variables. The one way analysis of variance was used to analyze the normally distributed data. The Kruskal-Wallis test was used to analyze the non-normally distributed data. The chi-square test and Fisher's exact test were used for the categorical variables. A p-value of <0.05 was considered statistically significant.

Results

The mean age of 4,247 patients who had undergone endometrial sampling at the Gynecology and Obstetrics Clinic of Konya Research and Training Hospital between January 2010 and October 2016 was 46.87±8.22 years, and the number of biopsies was observed to have increased each year. The most common indication for endometrial sampling was menometrorrhagia/menorrhagia, and it had been applied in 3,001 (70.66%) patients, followed by myoma uteri (n=456; 10.74%), post-menopausal bleeding or increased endometrial thickness (n=411; 9.68%), adnexal mass lesion (n=322; 7.58%), and cervical polyp (n=57; 1.34%) (Table 1).

The most common histopathological results were proliferative-secretory endometrium (n=2,701; 63.62%), endometrial polyp (n=444; 10.45%), simple hyperplasia without atypia (n=282; 6.65%), insufficient material (n=269; 6.33%), endometritis (n=204; 4.80%), atrophic endometrium (n=160; 3.77%), complex hyperplasia with atypia and endometrial adenocarcinoma (n=57; 1.34%), complex hyperplasia without atypia (n=48; 1.13%), and simple hyperplasia with atypia (n=24; 0.56%) (Table 2).

Of the 4,247 patients who had undergone endometrial sampling, 2,216 (52.18%) underwent hysterectomy. The comparison of hysterectomy and biopsy results is shown in Table 3. Although the histopathological results were found to be similar in 92.97% of the patients with proliferative-secretory endometrium, 88.52% of the patients with simple hyperplasia without atypia, 95.24% of the patients with complex hyperplasia without atypia, 95.83% of the patients with simple hyperplasia with atypia, 91.23% of the patients with complex hyperplasia with atypia, 83.29% of the patients with endometrial polyp, 93.48% of the patients with endometritis, 100% of the patients with endometrial adenocarcinoma, 84.50% of the patients with atrophic endometrium, and 75.68% of the patients with insufficient material, it was found to be different in 313 (14.13%) cases.

Discussion

We determined that 3,001 (70.66%) endometrial sampling procedures were most commonly performed with the indication of menometrorrhagia/menorrhagia; the most common histopathological finding was proliferative-secretory endometrium; 52.18% of the patients had undergone hysterectomy, and the histopathological results were the same as the biopsy results in 1,903 cases (85.87%) in our study, which included the analysis of endometrial biopsy results of 4,247 cases who had undergone endometrial sampling between January 2010 and October 2016.

Dysfunctional uterine bleeding is among the most common causes of admissions to the

Table 1. Distribution of the cases according to age and clinical indications

Years	Age (years)	Menometrorrhagia/ menorrhagia	Myoma uteri	Post-menopausal bleeding or increased endometrial thickness	Cervical polyp	Adnexal mass
2010 (734) (%)	47.05+8.05	532 (72.48)	50 (6.81)	68 (9.27)	11 (1.49)	73 (9.95)
2011 (429) (%)	47.21+9.07	303 (70.62)	38 (8.86)	36 (8.40)	9 (2.09)	43 (10.03)
2012 (522) (%)	47.53+8.14	389 (74.53)	41 (7.86)	41 (7.86)	6 (1.14)	45 (8.61)
2013 (482) (%)	47.22+7.87	332 (68.88)	48 (9.96)	44 (9.13)	9 (1.86)	49 (10.17)
2014 (584) (%)	46.44+7.98	413 (70.72)	71 (12.16)	69 (11.83)	77 (13.18)	24 (4.11)
2015 (685) (%)	45.99+8.00	464 (67.74)	95 (13.87)	69 (10.07)	8 (1.17)	49 (7.15)
2016 (811) (%)	46.96+8.64	568 (70.04)	113 (13.93)	84 (10.36)	7 (0.86)	39 (4.81)
Total 4,247 (%)	46.87+8.22	3,001 (70.66)	456 (10.74)	411 (9.68)	57 (1.34)	322 (7.58)

Table 2. Comparison of the indications and the histopathological results

	Age (Years)	Proliferative–secretory Endometrium	Simple Hyperplasia without atypia	Complex hyperplasia without atypia	Simple Hyperplasia with atypia	Complex hyperplasia with atypia	Endometrial polyp	Endometritis	Endometrial adenocarcinoma	Atrophic endometrium	Insufficient material
Menometrorrhagia/ menorrhagia (3,001) (%)	44.09+6.25	2,021 (67.35)	227 (7.57)	33 (1.09)	14 (0.46)	27 (0.89)	247 (8.24)	141 (4.70)	27 (0.89)	32 (1.07)	232 (7.74)
Myoma uteri (456) (%)	45.37+2.49	332 (72.80)	0	0	0	0	57 (12.5)	31 (6.79)	0	21 (4.61)	15 (3.29)
Post-menopausal bleeding or increased endometrial thickness (411) (%)	63.31+5.72	129 (31.39)	21 (5.11)	13 (3.16)	9 (2.19)	16 (3.90)	86 (20.92)	7 (1.70)	24 (5.84)	95 (23.11)	11 (2.68)
Cervical polyp (57) (%)	45.25+2.40	3 (5.26)	7 (12.28)	0	0	0	45 (78.95)	0	0	0	2 (3.51)
Adnexal mass (322) (%)	54.22+1.19	217 (67.40)	27 (8.39)	2 (0.62)	1 (0.31)	14 (4.35)	9 (2.79)	25 (7.76)	6 (1.86)	12 (3.73)	9 (2.79)
Total 4,247 (%)		2,702 (63.62)	282 (6.65)	48 (1.13)	24 (0.56)	57 (1.34)	444 (10.45)	204 (4.80)	57 (1.34)	160 (3.77)	269 (6.33)

Table 3. Biopsy and histopathological results of the patients who had undergone hysterectomy

	Proliferative–secretory endometrium	Simple hyperplasia without atypia	Complex hyperplasia without atypia	Simple hyperplasia with atypia	Complex hyperplasia with atypia	Endometrial polyp	Endometritis	Endometrial adenocarcinoma	Atrophic endometrium	Insufficient material
Biopsy Results (2,216)										
Proliferative–secretory endometrium (1.367) (%)	1.264 (92.47)	91 (6.66)	2 (0.15)	0	0	10 (0.72)	0	0	0	0
Simple hyperplasia without atypia (122) (%)	11 (9.02)	108 (88.52)	3 (2.46)	0	0	0	0	0	0	0
Complex hyperplasia without atypia (42) (%)	0	0	40 (95.24)	1 (2.38)	1 (2.38)	0	0	0	0	0
Simple hyperplasia with atypia (24) (%)	0	0	0	23 (95.83)	1 (4.17)	0	0	0	0	0
Complex hyperplasia with atypia (57) (%)	0	0	0	1 (1.75)	52 (91.23)	0	0	4 (7.01)	0	0
Endometrial polyp (335) (%)	44 (13.13)	11 (3.28)	1 (0.30)	0	0	279 (83.29)	0	0	0	0
Endometritis (46) (%)	0	3 (6.52)	0	0	0	0	43 (93.48)	0	0	0
Endometrial adenocarcinoma (57) (%)	0	0	0	0	0	0	0	57 (100)	0	0
Atrophic endometrium (129) (%)	0	2 (1.55)	0	0	0	0	18 (13.95)	0	109 (84.50)	0
Insufficient material (37) (%)	0	2 (5.40)	0	0	0	0	7 (18.92)	0	28 (75.68)	0
(2,216) (%)	1,319 (59.52)	217 (9.80)	46 (2.08)	25 (1.12)	54 (2.43)	289 (13.05)	68 (3.06)	61 (2.75)	137 (6.19)	0

Gynecology Outpatient Clinic and observed in approximately 20% of the women in reproductive age [8]. Causes such as endometrial polyp, endometrial hyperplasia, myoma uteri, and endometrial cancer (EC) should certainly be excluded beside systemic, iatrogenic, and hormonal causes in patients who present with dysfunctional uterine bleeding [8]. The main goal of endometrial sampling is to exclude EC [9], and endometrial sampling performed with the aim of controlling bleeding is controversial [10]. The gold standard method for verification of the diagnosis with endometrial biopsy is the histopathological assessment of the hysterectomy material [9].

Although the most common indication for endometrial biopsy was menometrorrhagia/ menorrhagia (70.66%) in our study, this rate may vary between 57% and 89% [1, 4, 6]. Routine endometrial sampling is not recommended before hysterectomy for exclusion of endometrial pathology in patients presenting with myoma uteri; however, it is still widely performed by many clinicians [5, 11]. In our study, EC was not determined in samples obtained due to myoma uteri, similar to the studies in the literature [6, 11].

Jetley et al. [12] determined proliferative-secretory endometrium in 63% of the patients who had undergone endometrial biopsy due to abnormal uterine bleeding, and Kucur et al. [6] determined this rate as 72.80%. We found this rate as 63.62%, consistent with the literature. The endometrial hyperplasia types with atypia, which may be simple, complex, or with or without atypia, are known to be precursor types of EC; cancer development

was reported as 1%-3% in hyperplasia without atypia and 8%-29% in hyperplasia with atypia [13]. The endometrial hyperplasia rate was reported as 9%-10% in endometrial samples obtained due to abnormal uterine bleeding in the studies of Kucur et al. [6] and Tuncer et al. [7]. Endometrial hyperplasia was found in 411 (9.68%) cases in our study.

Endometrial cancer is the most common gynecological cancer; 80% of the cases are seen in the post-menopausal period, and 95% of the patients present with abnormal uterine bleeding. The prevalence of EC varies between 2.5% and 6% in endometrial biopsies performed due to post-menopausal bleeding or endometrial thickness [14, 15]. We found this rate as 5.84% in our study, consistent with the literature.

The prevalence of endometritis varies between 3.2% and 9.1%; this rate was determined as 4.80% in our study, consistent with the literature [12, 16].

It is recommended that cervical polyps be removed routinely with concurrent endometrial sampling [17]. The presence of concurrent cervical polyp and endometrial polyp varies between 26.7% and 78.6% in the literature; we determined this rate as 78.95% in our study [1, 6].

Endometrial biopsy before the hysterectomy due for benign indications has become an indispensable routine procedure for clinicians. This biopsy procedure may lead to loss of labor, infection, or bleeding [5]. The consistency between the results of endometrial biopsy performed before hysterectomy and histopathological diagnosis is quite variable [18]. This rate was reported as 100% in cases with simple and complex hyperplasia, 47.1% in simple hyperplasia, 55%-60% in atrophic endometrium, 40%-60% in endometrial polyp, and 95% in EC [19-21]. Although biopsy results obtained before hysterectomy were found to be similar in 1,903 (85.87%) cases, they were different in 313 (14.13%) cases.

The potential weakness of this study is that it was conducted in a tertiary care institution and that it is a single-center study; the pathology specimens were not evaluated by a single pathologist. On the other hand, the large sample size may be the strength of the study.

In conclusion, while menometrorrhagia/menorrhagia is the most common indication for endometrial sampling, patients with post-menopausal bleeding or increased endometrial thickness were found to be most at risk for EC. While endometrial sampling should be performed following endometrial evaluation in post-menopausal patients, routine endometrial biopsy should not be performed in the other indications because it can increase the cost.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Konya Education and Research Hospital (2016-11-06).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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