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ARAŞTIRMA YAZISI / RESEARCH ARTICLE

HİSTEREKTOMİ YAPILAN KADINLARDA ENDOMETRİYAL BİYOPSİ VE KOLPOSKOPİ DESTEKLİ SERVİKAL BİYOPSİNİN TANI DOĞRULUĞU: TEK MERKEZ DENEYİMİ

DIAGNOSTIC ACCURACY OF ENDOMETRIAL SAMPLING AND COLPOSCOPY GUIDED CERVICAL BIOPSY IN WOMEN UNDERGOING HYSTERECTOMY: A SINGLE-CENTER EXPERIENCE

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ÖZET

AMAÇ: Bu çalışmanın amacı, ameliyat öncesi alınan endometriyal ve servikal biyopsi sonuçlarını, ilgili histerektomi örneklerinin histopatolojik özellikleriyle karşılaştırmak ve böylece tutarlılıklarını araştırmaktır.

GEREÇ VE YÖNTEM: Bu çalışma, 1 Ocak 2017 ile 1 Ocak 2023 tarihleri arasında çalışma merkezinde servikal ve endometriyal biyopsilerle doğrulanan, benign ve malign endikasyonlarla gerçekleştirilen 390 histerektominin retrospektif bir incelemesidir.

BULGULAR: Yetmiş dört histerektominin (%19,0) preoperatif servikal biyopsi sonucu, 316 histerektominin ise preoperatif endometriyal biyopsi sonucu (%81,0) vardı. Benign lezyonlar için endometriyal biyopsi sonuçları ile ilgili histerektomi örnekleri arasında yalnızca %55,6 uyum (κ=0,011) vardı ve anlamlı korelasyon yoktu (χ2=4,500, p=0,343). Preinvaziv ve malign lezyonlar için servikal biyopsi sonuçları ile ilgili histerektomi örnekleri arasında %85,1 uyum (κ=0,462) ve anlamlı korelasyon vardı (χ2=106,349, p=0,001). Polipleri ortaya koyan endometriyal biyopsi sonuçları 59,3 ile en düşük tanısal doğruluğa sahipti. Biyopsi sonuçlarında atipili kompleks hiperplazi saptanan hastaların %52,2'sinde endometriyal kanser tespit edildi.

SONUÇ: Endometriyal biyopsinin göreceli olarak daha düşük tanısal doğruluğu, benign endikasyonlarla histerektomi planlanan hastalarda kesin tanı için gerekli olmadığını düşündürmektedir. Kompleks atipik hiperplazi ve endometriyal kanserin birlikte görülme oranının göreceli olarak daha yüksek olması, biyopsi bazlı hiperplazisi olan hastalarda histerektomi planlanmadan önce rahim boşluğunun görüntülenmesi için histeroskopi yapılabileceğini de göstermektedir. Servikal biyopsi sonuçları ile ilgili histerektomi örnekleri arasındaki uyum oranının nispeten yüksek olması serviksin pre-invaziv ve malign lezyonlarının tedavisinde kolposkopinin önemini ve geçerliliğini desteklemektedir.

ANAHTAR KELİMELER: Biyopsi, Teşhis, Histerektomi, Patoloji.

ABSTRACT

OBJECTIVE: This study aims to compare the results of the preoperatively obtained endometrial and cervical biopsies to the histopathological characteristics of the related hysterectomy specimens and, thus in vestigate their consistency.

MATERIAL AND METHODS: This is a retrospective review of 390 hysterectomies performed for both benign and malignant indications as verified by cervical and endometrial biopsies at the study center between 1 January 2017 and 1 January 2023.

RESULTS: Seventy-four hysterectomies (19.0%) had preoperative cervical biopsy results, while 316 had preoperative endometrial biopsy results (81.0%). Only 55.6% agreement (κ=0.011) and no significant correlation between endometrial biopsy results and related hysterectomy specimens for benign lesions (χ2=4.500, p=0.343). There were 85.1% agreement (κ=0.462) and a significant correlation between cervical biopsy results and related hysterectomy specimens for pre-invasive and malignant lesions (χ2=106.349, p=0.001). Endometrial biopsy results presenting polyps had the lowest diagnostic accuracy of 59.3% and endometrial cancer was identified in 52.2% of the patients whose biopsy results revealed complex hyperplasia with atypia.

CONCLUSIONS: The relatively lower diagnostic accuracy of endometrial biopsy suggests that it is not required for definitive diagnosis in patients who are scheduled to have a hysterectomy for benign indications. The relatively higher rate of complex atypical hyperplasia and endometrial cancer co-existence also indicates that hysteroscopy can be performed to visualize the uterine cavity before a hysterectomy is planned for patients with biopsy-based hyperplasia. The relatively higher concordance rate between cervical biopsy results and related hysterectomy specimens supports the significance and validity of colposcopy in the management of pre-invasive and malignant lesions of the cervix.

KEYWORDS: Biopsy, Diagnosis, Hysterectomy, Pathology.

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INTRODUCTION

Hysterectomy refers to the removal of the uterus surgically. This operative procedure is the most performed gynecological surgery worldwide (1). Hysterectomy can be carried out for benign and malignant indications. Benign indications such as uterine leiomyomas and abnormal vaginal bleeding constitute the major reason for hysterectomies (1, 2). On the other hand, malignant indications for hysterectomy predominantly consist of gynecological tumors (3). Each hysterectomy sample should be examined histopathologically as histological findings are considered the main basis for the ultimate diagnosis (4, 5).

Being a major indication for hysterectomy, abnormal uterine bleeding has a variety of underlying etiologies including fibroids, endometrial polyp, endometrial hyperplasia, adenomyosis, infectious diseases, early pregnancy complications, and malignancies (6). Endometrial biopsy is usually performed to identify the underlying etiology of abnormal uterine bleeding as this method allows the efficient sampling of endometrium and its quick analysis (7). Since endometrial cancer is the fourth most frequent cancer among women, endometrial biopsy should be performed essentially in all women with abnormal uterine bleeding (8, 9). It has been reported that endometrial biopsy procedure has a high sensitivity and specificity for detecting endometrial hyperplasia and endometrial malignancy. Therefore, endometrial biopsy remains the first-line tool for diagnostic workup of abnormal uterine bleeding (10, 11).

As for the diagnosis of cervical intraepithelial neoplasms and cervical cancer, colposcopy-guided cervical biopsy has been designated as the gold standard. Besides, histopathology has been addressed as the reference standard for specifying the treatment and subsequent follow-up in women with premalignant and malignant cervical lesions (12, 13).

This study aims to compare the results of the preoperatively obtained endometrial and cervical biopsies to the histopathological characteristics of the related hysterectomy specimens and, thusinvestigate their consistency.

MATERIALS AND METHODS

Written informed consent was obtained from each participant. This is a retrospective review of 1311 hysterectomies which were performed for both benign and malignant indications at the study center between 1 January 2017 and 1 January 2023. The hysterectomies with unknown or absent preoperative biopsy results and the hysterectomies with endometrial biopsy results announced more than two months before surgery were excluded. Therefore, 390 hysterectomies (29.7%) were included. Endometrial biopsy was done by using the dilatation and curettage (D&C) technique. In this technique, the patient was put into a dorsal lithotomy position and then general anesthesia or paracervical block was performed. After the perineum and vagina were cleansed, the cervix was dilated with small Hegar dilators. Then, the uterine cavity was achieved and evacuated.

A cervical biopsy was acquired under the guidance of colposcopy. Before colposcopic observation was begun, the cervical surface was cleaned with saline, and all secretions were wiped away. Afterward, the cervix was carefully examined by colposcopy, and cervical tissue was stripped by punch biopsy forceps at the site of a colposcopic lesion. All histological sections derived from hysterectomy specimens and endometrial and cervical biopsies were fixed in formalin, embedded in paraffin, cut into 5-mm-thick sections, and stained with hematoxylin and eosin for histopathological examination.

Ethical Committee

The present study is approved by the ethical committee of Afyonkarahisar Health Sciences University where it was undertaken (Grant no:2023/10).

Statistical Analysis

Collected data were analyzed by Statistical Package for Social Sciences version 22.0 (SPSS, SPSS IBM., Armonk, NY, USA). Categorical data were denoted as numbers and percentages. Sensitivity, specificity, positive and predictive values, and diagnostic accuracy were calculated for biopsy results. Chi-square test was used to assess the correlations and Cohn's Kappa test was used to evaluate the concor-

dance between preoperative and postoperative histological findings. Two-tailed p values <0.05 were accepted as statistically significant.

RESULTS

Three hundred sixteen hysterectomies had preoperative endometrial biopsy results (81.0%). Twenty-seven hysterectomies (8.5%) had preoperative endometrial biopsy results that reported benign lesions. Our research shows that there is only 55.6% agreement (κ=0.011) and no statistically significant correlation between endometrial biopsy results specifying benign lesions and related hysterectomy specimens(χ2=4.500, p=0.343) **(Table 1)**.

Table 1: Correlation of benign endometrial biopsy results and hysterectomy findings

		Hysterectomy specimen				
		Polyp	Benign changes	Simple hyperplasia without atypia	Simple hyperplasia with atypia	Endometrial cancer
Endometrial biopsy	Polyp	13	7	1	1	2
	Benign changes	-	2	-	-	1
Total		13	9	1	1	3

Histopathological examination revealed more severe findings in the hysterectomy specimens of 5 patients (18.5%) who had endometrial biopsy results reporting benign lesions. A total of 289 hysterectomies (91.5%) had preoperative endometrial biopsy results which included pre-malignant and malignant lesions. This study demonstrates that there is 77.5% agreement (κ=0.357) and a significant correlation between endometrial biopsy results pointing out pre-malignant and malignant lesions and related hysterectomy specimens (x2=793.906, p=0.001) **(Table 2)**.

Table 2: Correlation of premalignant and malignant endometrial biopsy results and hysterectomy findings

		Hysterectomy							
		Simple hyperplasia without atypia	Simple hyperplasia with atypia	Complex hyperplasia without atypia	Complex hyperplasia with atypia	Polyp	Benign changes	Endometrial cancer	Uterine sarcoma
Endometrial biopsy	Simple hyperplasia without atypia	11	1	-	1	4	12	-	-
	Simple hyperplasia with atypia	-	2	-	1	-	1	-	-
	Complex hyperplasia without atypia	-	-	1	-	-	-	-	-
	Complex hyperplasia with atypia	6	2	-	11	-	3	24	-
	Endometrial cancer	-	1	-	4	-	-	186	4
	Uterine sarcoma	-	-	-	-	-	-	1	13
Total		17	6	1	17	4	16	211	17

Seventy-four hysterectomies (19.0%) had preoperative cervical biopsy results. These results display that there is 85.1% agreement (κ=0.462) and a significant correlation between cervical biopsy results pointing out pre-invasive and malignant lesions and related hysterectomy specimens (x2=106.349, p=0.001) **(Table 3)**.

Table 3: Correlation of cervical biopsy results and hysterectomy findings

		Hysterectomy			
		Cervicitis	Low grade cervical intraepithelial lesion	High grade cervical intraepithelial lesion	Cervical cancer
Cervical biopsy	Low grade intraepithelial lesion	-	8	-	-
	High grade intraepithelial lesion	3	2	34	5
	Cervical cancer	1	-	-	21
Total		4	10	34	26

Table 4 summarizes the diagnostic power of biopsy results. Endometrial biopsies specifying polyps had the highest sensitivity of 100.0% and the lowest specificity and diagnostic accuracy of 21.4% and 59.3% respectively. Those describing complex hyperplasia with atypia had the lowest sensitivity of 64.7%, specificity of 88.2%, and diagnostic accuracy of 87%. Endometrial cancer was identified in 52.2% of the patients whose biopsy results revealed complex hyperplasia with atypia. Cervical biopsy results presenting high-grade intraepithelial lesion (HSIL) had the highest sensitivity of 100.0%, specificity of 74.4%, and diagnostic accuracy of 86.3%. Those describing low-grade intraepithelial lesions (LSIL) had a sensitivity of 80.0%, the highest specificity, and diagnostic accuracy of 100.0% **(Table 4)**.

Table 4: Diagnostic power of endometrial and cervical biopsy results

	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Diagnostic accuracy
Endometrial polyp	100.0%	21.4%	54.2%	100.0%	59.3%
Simple hyperplasia without atypia	64.7%	93.4%	37.9%	97.7%	91.7%
Complex hyperplasia with atypia	64.7%	88.2%	25.6%	97.6%	86.9%
Endometrial cancer	88.2%	88.5%	95.4%	73.4%	88.2%
Uterine sarcoma	76.5%	99.6%	92.9%	98.5%	98.3%
Low grade cervical intraepithelial lesion	80.0%	100.0%	100.0%	100.0%	100.0%
High grade cervical intraepithelial lesion	100.0%	74.4%	77.3%	100.0%	86.3%
Cervical cancer	80.8%	97.9%	95.5%	90.2%	91.8%

DISCUSSION

Routine endometrial sampling before hysterectomy has been a matter of debate (7, 10). Therefore, this study has been designed to investigate the compatibility between endometrial biopsy results and histopathological findings in related hysterectomy specimens.

The present study claims that there is only 55.6% agreement between endometrial biopsy results pointing out benign lesions and related hysterectomy specimens. Thus, endometrial biopsy re-

sults revealing polyp had the highest sensitivity of 100.0% and the lowest specificity and diagnostic accuracy of 21.4% and 59.3% respectively.

Moreover, histopathological analysis revealed more severe findings in the hysterectomy specimens of 4 patients (16.7%) who were diagnosed with polyps according to endometrial biopsy.

Preoperative endometrial biopsy was able to detect none of the polyps in a cohort of 163 women who had hysterectomy (14). The agreement between endometrial biopsy and hysterectomy specimens was 58.3% for polyps in another cohort of 43 women (15). These findings comply with the well-established recommendation D&C should be avoided as it is not suitable for the management of endometrial polyps (16, 17). It has been hypothesized that this inconvenience is due to the focal growth behavior of polyps (18). This focal growth behavior may also lead to skipping in the diagnosis of pre-malignant and malignant lesions that accompany endometrial polyps. It has been concluded that the prevalence of concurrent pre-malignancy and malignancy changes between 0% and 13% in patients with polyps (19, 20). Interestingly, an Iranian study eventually detected endometrial hyperplasia in two women (16.7%) who were diagnosed with endometrial polyps by D&C technique (15).

In this study, the agreement rate between preoperative and postoperative histological findings was 77.5% for pre-malignant and malignant endometrial lesions. Endometrial biopsy results presenting complex hyperplasia with atypia had the lowest sensitivity of 64.7%, specificity of 88.2%, and diagnostic accuracy of 87%. The agreement between preoperative and post-operative histological findings was 59.1% for pre-malignant and malignant endometrial lesions in a sample of 43 patients who underwent hysterectomy (15). On the other hand, there was 72.5% consistency between preoperative and post-operative histological findings for endometrial hyperplasia and cancer in a relatively large cohort (21). The sensitivity of D&C was computed to be 62.5% for the diagnosis of endometrial hyperplasia in another sample of 163 patients (14).

This study identified endometrial cancer in 52.2% of the patients who had complex hyperplasia with atypia according to endometrial biopsy results. This finding complied with the study of Kurt et al. (22) who detected endometrial cancer as 44.7% in a sample of 58 patients who had hysterectomy due to endometrial hyperplasia. Another review of 2571 patients determined the prevalence of endometrial cancer as 37% in hysterectomy specimens of the patients who have been previously diagnosed with atypical endometrial hyperplasia (23). The prevalence of endometrial cancer was 25.1% in an assessment of 227 women who had hysterectomy for atypical hyperplasia (24). This prevalence even decreased to 10.3% in another similar evaluation of 126 hysterectomy specimens (25). On the contrary, none of the patients with atypical hyperplasia obtained the eventual diagnosis of endometrial cancer after hysterectomy whereas 73.7% of the patients who had complex atypical hyperplasia received the final diagnosis of endometrial cancer after hysterectomy in a Mexican study (26). This contradiction about the upgrading rate of endometrial hyperplasia might be attributed to the varying efficiency of sampling and histopathological examination techniques.

Endometrial biopsy results reporting cancer had a sensitivity and diagnostic accuracy of 88.2% in this study. This value was by a previous study which underlined the sensitivity of D&C as 83.3% in the diagnosis of endometrial cancer (14). Similarly, a meta-analysis of 1607 participants concluded that the conventional D&C technique had a sensitivity of 88% for the diagnosis of endometrial cancer (27).

Colposcopy is frequently used for the diagnosis of cervical lesions because colposcopic biopsies provide the histopathological background for the diagnosis, treatment, and follow-up of cervical lesions (28). However, there are limited and controversial data about the accuracy of colposcopy-guided cervical lesions. That is, the concordance rate changed from 45% to 90% for cervical biopsy results and related conization specimens (29, 30).

As for the present study, there was 85.1% agreement between cervical biopsy results and related hysterectomy specimens for pre-invasive and malignant lesions. This rate resembled the consistency rate of 83.3% between

cervical biopsies and conization specimens as declared by a review of 2681 patients (31).

In this study, HSIL was downgraded to LSIL in 4.5% of 44 patients and upgraded to cervical cancer in 11.4% of them. Yet, the diagnostic accuracy of LSIL was 100% in colposcopy-guided cervical biopsies. This was in contrast to a prior German study which claimed that the diagnostic accuracy of high-grade lesions was significantly higher than that of low-grade lesions (78.5% vs 33.3%). The same study also designated HSIL for the conization specimens in 18% of 266 patients who were formerly diagnosed with LSIL by colposcopy (32). Such discrepancy in the diagnostic accuracy of colposcopy-guided biopsy might be linked to age, menopause, involvement of transformation zone, and severity of cervical lesions.

In conclusion, the relatively lower diagnostic accuracy of D&C in patients with benign pathologies suggests that endometrial biopsy is not required for definitive diagnosis in patients who are scheduled to have a hysterectomy for benign indications. The relatively higher rate of the complex atypical hyperplasia and cancer co-existence in this study also indicates that hysteroscopy can be performed to visualize the uterine cavity before a hysterectomy is planned for patients with biopsy-based hyperplasia. Moreover, the patients who are to undergo hysterectomy for complex endometrial hyperplasia with atypia should be informed about the malignancy risk and a frozen section procedure should be carried out in these patients.

This study also highlights the relatively higher concordance rate between cervical biopsy results and related hysterectomy specimens supports the significance and validity of colposcopy in the management of pre-invasive and malignant lesions of the cervix. However, these conclusions should be interpreted carefully as their power is limited by relatively small cohort size, retrospective study design, and heterogeneity in demographic and clinical characteristics. The variations in histopathological sampling and inspection techniques might have also caused bias. Further research has been warranted to clarify the compatibility between preoperatively obtained cervical and endometrial biopsies and related hysterectomy specimens.

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