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Diagnostic Role of Hysteroscopy In Women With Abnormal Uterine Bleeding: A Single-Center Retrospective Study

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ABSTRACT

Hysteroscopy is a minimally invasive technique that has advantages over blind curettage, such as direct visualization of the intrauterine cavity, biopsy of the suspicious area, and simultaneous treatment of benign intracavitary lesions. The study aims to evaluate the diagnostic role of hysteroscopy in endometrial and focal intracavitary lesions.

This retrospective study was conducted in the department of obstetrics and gynecology of a tertiary center between January 2018 and July 2022. Diagnostic hysteroscopy was performed on women with abnormal uterine bleeding, and lesions seen during hysteroscopy were noted and excised using a resectoscope. Uterine sampling with blind curettage was applied to all patients. The resected lesions and uterus samples were evaluated histopathologically.

Diagnostic accuracy of hysteroscopy was higher than 90% in each group classified according to morphology of endometrium as normal, atrophic and hyperplastic. Sensitivity, specificity and diagnostic accuracy were higher than 90% for focal intracavitary pathologies. Sensitivity for endometrial hyperplasia and cancer were 80% and 50%, respectively.

Hysteroscopy is exceedingly viable for distinguishing intracavitary pathologies such as polyps, myomas and foreign bodies in ladies with abnormal uterine bleeding. However, for the diagnosis of endometrial hyperplasia and cancer, a hysteroscopy-guided biopsy with uterine curettage is needed to be combined with hysteroscopy.

Keywords: Abnormal uterine bleeding, Endometrium, Hysteroscopy, Uterine curettage, Uterine intracavitary pathology

Introduction

Abnormal uterine bleeding (AUB) is a health problem that affects millions of women worldwide. Gynecologic or non-gynecologic pathologies may lead to AUB during reproductive years or at menopause (1). The best methods to begin evaluating AUB are a thorough history and physical examination. Anovulatory bleeding can be defined as infrequent, irregular, unpredictable menstrual bleeding that varies in quantity, duration, and character, is not accompanied by any palpable or visible abnormalities of the genital tract, and is not preceded by any identifiable or consistent pattern of premenstrual molimina. On the other hand, heavy or protracted menstrual periods are more likely to be caused by a bleeding condition or an anatomical injury than by anovulation (2). The causes of AUB reported by FIGO include polyps, adenomyosis, leiomyoma, malignancy and hyperplasia, ovulatory dysfunctions, endometrial, coagulopathy, iatrogenic and those not yet classified. Of these, uterine intracavitary pathologies such as polyp, adenomyoma, leiomyoma, malignancy and hyperplasia constitute the largest group and can be diagnosed by imaging and/or histopathology (3).

As a feasible and non-invasive technique, the first step for detecting intracavitary pathologies is transvaginal sonography (TVS). However, a

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definitive diagnosis is not achieved with TVS alone (4). Especially in lesions in the uterine cavity and various endocervical and endometrial pathologies, saline infusion sonography, which uses the same principles as ultrasound, is a widely used imaging method for imaging endometrial lesions and especially for evaluating space-occupying lesions in the uterine cavity, with similar sensitivity to hysteroscopy (5). Histopathologic confirmation which is the gold standard is needed to establish the diagnosis (4,6).

Uterine curettage is a conventional, cost-effective and easy method used sampling endometrium for histopathology. The necessity for hospitalization and general or local anesthetic services, the high risk of complications, the low diagnostic yield (many focal lesions are missed), and the total lack of any therapeutic role are only a few of the technique's demonstrated serious drawbacks (7). In contrast to dilatation and curettage, hysteroscopy is not blind and can be performed in an office setting. A trustworthy technique for identifying intrauterine anomalies is hysteroscopic evaluation, which enables direct vision and assessment of the endocervical and uterine cavities (8).

It is important to take an appropriate sample when performing an endometrial biopsy. In patients with suspected endometrial malignancy, hysteroscopic evaluation and, if necessary, hysteroscopy-guided biopsies are more valuable than uterine curettage alone and are the targeted biopsy method with the highest diagnostic accuracy. It is also offered as a minimally invasive technique to patients with AUB, with the advantages of providing simultaneous treatment for benign intracavitary lesions under direct vision (9-12).

The aim of this study is to evaluate the diagnostic potential of hysteroscopy in cases of AUB, considering the correlation with histopathology.

Material and Methods

The study was conducted after the Institutional Ethical Board Committee (E-46059653-020) approved the study to be conducted in the Department of Gynecology and Obstetrics of University of Health Sciences, Sancaktepe Sehit Prof. Dr. Ilhan Varank Training and Research Hospital, Istanbul, Turkey between January 2018 and July 2022. The study complied with the Declaration of Helsinki Principles. Written informed consent was obtained from all women prior to the study.

This retrospective study included 232 women aged 19-76 who applied to our clinic with AUB complaints. AUB was diagnosed according to the FIGO classification system (PALM-COEIN) (13,14). All patients underwent hysteroscopy followed by uterine curettage. Inclusion criteria were AUB in women in reproductive and peri-postmenopausal age group. Exclusion criteria were pregnancy, pelvic inflammatory disease, benign pelvic pathologies (adnexal masses, fibroids), endometrial, cervical and vaginal cancer, medical treatment of endometrial hyperplasia (oral or combined progestin therapy with levonorgestrel-releasing intrauterine device), tamoxifen treatment and coagulation disorders.

Hysteroscopies were scheduled at the follicular phase of menstrual cycle or at the period without bleeding for postmenopausal women following routine gynecologic examination and TVS scans. AUB was determined as different from normal menstrual pattern for premenopausal women and bleeding after at least one-year of cessation for postmenopausal women.

All procedures were performed by the specialists in gynecology. Diagnostic hysteroscopy was performed with a 5mm and 30°hysteroscope (Karl Storz, Germany) under general anesthesia. Mannitol 5% solution was used for distention of the uterine cavity that would allow unipolar resectoscope to perform if necessary.

Endometrium was classified as normal, atrophic and hyperplastic according to the hysteroscopic view and noted. Suspicion of cancer or infection was also noted. Resection of focal intracavitary pathologies was performed with a 10mm and 12° resectoscope (Karl Storz, Germany). Lesions were identified as polyps, myoma, adenomyoma and foreign bodies according to their hysteroscopic view and noted. All patients first underwent hysteroscopy, the uterine cavity was visualized and visual lesions were identified and the preliminary diagnosis was noted, then blind uterine curettage was performed and endometrial samples were taken for histopathological evaluation.

Hysteroscopic identification of endometrium and intracavitary pathologies was based on the following definitions:

Normal endometrium: Thin and regular, pink-colored endometrium (proliferative) or thick and undulating, orange-colored endometrium (secretory).

Hyperplastic endometrium: Thick, undulating, irregular or edematous endometrium.

Atrophic endometrium: Thin, flat, fragile and pale-colored or petechial hemorrhagic endometrium.

Endometrial cancer: Diffuse hyperplastic/normal, hypervascular and focal hemorrhagic/ulcerous or focal hypervascular, edematous and hemorrhagic/ulcerous endometrium.

Endometrial polyp: Soft, oval, pink-colored and pedunculated lesions.

Submucous myoma: Firm, round, white-colored, pedunculated/partially intramural lesions.

Adenomyoma: Fibrous, cystic and white or hemorrhagic, cystic, blue/chocolate brown-colored lesions.

Resected lesions and endometrial samplings were sent for histopathologic evaluation and results were recorded.

Statistical analysis: Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy of hysteroscopy of the endometrium and focal intracavitary pathologies were calculated with a 95% confidence interval. Medcalc statistical software, 2017 Belgium was used for statistical calculations. Finally, we used G*Power version 3.1 (Heinrich Heine University, Germany) to perform a post-hoc assessment of the power analysis. We calculated the power of our study (1-β) considering the number of patients who underwent hysteroscopy and histopathology, with an error of α of 0.05, assuming the diagnostic rates in the two groups as the main outcome measure (8).

Results

A total of 266 people applied with complaints of abnormal uterine bleeding between the dates of the study, all applications were evaluated and 34 people who received hyperplasia treatment were excluded from the study. A total of 232 women were included in the study. During hysteroscopy, the intrauterine endometrium could not be visualized in 3 women due to inappropriate phases. Therefore, the hysteroscopic evaluation of 3 patients could not be noted. The majority of the patients included in the study were multiparous 67.3% (n=156), the most common symptom was pelvic pain 37.1% (n=86). Also, the most common TVUSG finding was polyp 56.4% (n=131). Other demographic variables are shown in (Table 1). Hysteroscopic evaluation could detect normal endometrium in 175 of 189 women who had histopathologically proven to have normal endometrium. Fifteen false positive and 1 false negative were obtained with hysteroscopy. The Histopathologic diagnosis of the false negative case was simple hyperplasia. Nine and 6 of 15 false positive normal endometria were viewed as hyperplastic and atrophic, respectively (Table 2).

Five women had histopathologically proven hyperplastic endometrium. Hysteroscopic evaluation could detect four of those. One had normal endometrium as examined. In 2 patients, endometrial cancer was detected on that hyperplastic base. One of the two was endometrioid cancer which was not seen as suspicious and the other was adenocarcinoma with hypervascular and hemorrhagic suspicious areas hysteroscopically. In the other 2 patients with endometritis, simple hyperplasia and atypical complex hyperplasia were detected with histopathology. In 7 women showing hyperplastic endometrium, histopathology was found to be normal.

In 34 of 38 patients, atrophy revealed from histopathology correlated with hysteroscopy. However, 7 false positive and 4 false negatives were found. Endometritis was not identified in hysteroscopy (Table 2). The diagnostic accuracy of identifying normal endometrium with hysteroscopy was found 93%. Sensitivity, specificity, NPV and PPV were 92%, 98%, 74%, and 99%; respectively. Moreover, sensitivity, specificity, PPV, NPV and diagnostic accuracy of hysteroscopy for hyperplastic endometrium were 80%, 97%, 33%, 100% and 96%, respectively. Sensitivity, specificity, PPV, NPV and diagnostic accuracy of other parameters for hysteroscopic evaluation of endometrium were calculated as shown in (Table 3).

One hundred and twenty-five lesions identified as polyp were resected with hysteroscopy. One hundred and nineteen were correlated with histopathology. Four polyps were not identified while 6 false positives were obtained. Three polyps were suspicious in view and histopathology revealed malignity in all three (atypic complex hyperplasia, clear cell carcinoma and endometrioid carcinoma). One polyp had focal simple hyperplasia, but no typical appearance was found with hysteroscopy.

Seventeen of eighteen myomas diagnosed with histopathology were also identified with hysteroscopy. One viewed myoma was proved a fibrous polyp. One histopathologic-proven adenomyoma was diagnosed hysteroscopically. Five embedded foreign bodies (intrauterine device

Table 1: Demographic Variables of Patients

Patient characteristics	n=232 (%)
Age (year)	19-76
Parity	
Multipara	156 (67%)
Primipara	36 (16%)
Nullipara	40 (17%)
Associated symptom	
Pelvic pain	86 (37%)
Infertility	49 (21%)
Dyspareunia	16 (7%)
Associated disease	
Diabetes	18 (8%)
Hypertension	33 (14%)
Thyroid disorder	26 (11%)
Breast cancer	6 (3%)
Crohn's disease	1 (0.4%)
TVS findings	
Normal	37 (16%)
Thick/irregular endometrium	50 (22%)
Submucous myoma	23 (10%)
Polyp	131 (56%)
Foreign body	5 (2%)

TVS: Transvaginal Sonography

Table 2: Hysteroscopic and Histopathologic Evaluation of Endometrium

Endometrium	Hysteroscopy (n)	Histopathology (n)	Correlation (n)
Normal	175	189	174
Hyperplastic	12	5	4
Atrophic	41	38	34
Endometritis	0	2	0
Endometrial cancer	1	2	1

fragments) were found and removed except for one (Table 4).

Discussion

With the contribution of developing technology, the importance of modern hysteroscopy for the management of endometrial pathology has significantly increased (9,12). In this study, to evaluate the diagnostic potential of hysteroscopy, identifications made on hysteroscopic views were assessed according to histopathologic results.

The diagnostic accuracy of identifying normal endometrium with hysteroscopy was found 93%. Sensitivity, specificity, NPV and PPV were 92%, 98%, 74%, and 99%; respectively. The literature has reported similar results (15,16). According to the results, direct visualization of the cavity seems to provide adequate identification of normal endometrium.

Sensitivity, specificity and diagnostic accuracy in viewing myoma were similar to the literature, as 100%, 100%, 100% respectively (17).

Hyperplasia has no typical appearance. Thick and undulating normal endometrium can mimic hyperplasia and hyperplasia may be identified as polypoid endometrium (17). We found eight false positive hyperplasia in hysteroscopy and lower PPV than reported values in the most previous studies (18,19). According to the results, sensitivity, specificity, PPV, NPV and diagnostic accuracy of hysteroscopy for hyperplastic

Table 3: Diagnostic Accuracy of Hysteroscopy for Endometrium

Hysteroscopy (%95 CI)	Sensitivity (%)	Specificity (%)	PPV* (%)	NPV** (%)	Accuracy (%)
Normal	92 (87.25-95.49)	98 (87.71-99.94)	99 (96.16-99.92)	74 (63.22-82.02)	93 (89.04-96.01)
Hyperplastic	80 (28.36-99.49)	97 (94.34-99.02)	33 (21.27-62.19)	100 (97.45-99.92)	96 (93.88-98.78)
Atrophic	90 (75.20-97.06)	96 (86.95-99.21)	83 (56.76-77.48)	98 (94.62-99.12)	100 (87-100)
Endometritis	0	100 (98.41-100)	-	99 (99.14-99.14)	99 (96.92-99.90)
Endometrial cancer	50 (1.26-98.74)	100 (98.41-100)	100	100	100
Polyp	97 (91.88-99.11)	91 (88.40-97.95)	92 (90.10-97-74)	96 (90.75-98-54)	94 (92.22-97.91)
Polyp with focal malignity	100 (29.24-100)	100 (98.40-100)	100	100	100 (98.42-100)
Myoma	100 (80.49-100)	100 (97.44-99.99)	94 (70.64-99.17)	100	100 (97.62-99.99)
Adenomyoma	100	100	100	100	100 (98.42-100)
Foreign body	100	100	100	100	100

*Positive Predictive Value
**Negative Predictive Value

Table 4: Hysteroscopic and Histopathologic Evaluation of Intracavitary Lesions

LESIONS	Hysteroscopy (n)	Histopathology (n)	Correlation (n)
Polyp	125	123	119
Polyp with focal malignity	3	3+(1)*	3
Myoma	18	17	17
Adenomyoma	1	1	1
Foreign body	5	-	-

*Polyp with focal simple hyperplasia

endometrium were 80%, 97%, 33%, 100% and 96%, respectively. The relatively low sensitivity and an obviously low PPV per se in identification hyperplasia preclude its use for diagnostic purposes alone without an accompanying biopsy or sampling curettage, especially in women with high preoperative suspicion. A meta-analysis in 2015 reported that hysteroscopy was more useful to exclude hyperplasia than to prove it and the low NPV in the presented study is in accordance with this conclusion since only 40% of proven hyperplasia could be detected with direct hysteroscopic view (18).

Endometrial cancer was diagnosed in two patients showing hyperplastic endometrium. Only one had a suspicion on of hysteroscopy, which means the sensitivity of hysteroscopic viewing for diagnosis of endometrial cancer was 50%. However, the small sample size in this study restricts the validity of this rate. Researches have reported that none of the four endometrial cancers caused suspicious hysteroscopic findings in their 134 patients' group (17). Some other studies also reported low sensitivity of hysteroscopy for hyperplasia and cancer (20). As for hyperplasia, the low sensitivity of hysteroscopy itself in detecting cancer precludes its use for diagnostic purposes alone

without an accompanying biopsy or sampling curettage.

Histopathologic evaluation is considered the gold standard for diagnosis and necessary for appropriate treatment. However, uterine curettage alone may fail in more than 50% of the cases to detect the malignity (7). Hysteroscopic-guided biopsies may be more valuable than uterine curettage alone. In this study, although malignity was proven in three polyps having suspicion in hysteroscopy, blind uterine curettage found cancer in only one. Similar to the literature, we found sensitivity, specificity and diagnostic accuracy of hysteroscopy for polyps with focal malignity in all 100%, respectively (21,22).

The most seen intracavitary pathology causing AUB was endometrial polyp in this study. Polyps, submucous myomas (except one), embedded IUD fragments and a chocolate-colored, cystic adenomyoma were diagnosed and removed with hysteroscopy at the same session. High sensitivity, specificity and diagnostic accuracy, which were comparable to other studies, were found for all focal lesions (11,16,19,21). Hysteroscopy seems to be a highly effective method to diagnose and treatment for benign focal intracavitary pathologies.

The methodological limitations of this research are disadvantages for the patient to receive general anesthesia and due to the limited resources and limited settings, we do not have office hysteroscopy, further studies should focus on office hysteroscopy in their pathological comparing studies. Another limitation is that although we make definitions, observation of the uterine cavity and diagnosis during hysteroscopy are subjective data that require experience.

In conclusion, hysteroscopic evaluation of the uterine cavity under direct vision is highly accurate in identifying normal and atrophic endometrium. Moreover, hysteroscopy also provides the accurate diagnosis and simultaneous treatment for benign focal intracavitary pathologies such as polyps, myomas and foreign bodies. However, for the diagnosis of endometrial hyperplasia and cancer, a hysteroscopy-guided biopsy with uterine curettage is needed to be combined with hysteroscopy.

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