



Comparison of Diagnostic Techniques Used in the Differential Diagnosis of Endometrial Pathologies Presenting with an Abnormal Uterine Bleeding

Anormal Rahim Kanaması ile Başvuran Endometrial Patolojilerin Ayırıcı Tanısında Farklı Tanı Tekniklerinin Karşılaştırılması

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Abstract

Aim: Transvaginal ultrasonography (TVUSG) examination, dilatation and curettage (D&C) approach and hysteroscopic assesment are frequently used in examination of the abnormal uterine bleeding (AUB). The specisific test for detection of the AUB is histopathological evaluation. The study aimed to check the exactness of TVUSG, D&C and hysteroscopy for differential diagnosis of the AUB.

Material and Method: Subjects with AUB, who were supposed to have an endometrial pathology on TVUSG, D&C or hysteroscopy, were included in this retrospective study. Our retrospective study was conducted in 160 patients who were admitted to our clinic with complaint of abnormal uterine bleeding. The final pathological diagnosis was accepted as the reference test and sensitivity and specifity of the D&C, hysteroscopy and TVUSG was checked with the pathological diagnosis.

Results: Hysteroscopy combined with biopsy provided highest correlation with the histopathological evaluation. However, the statistical values obtained with TVUSG was comparable to that of the hysteroscopy alone and D&C but lower than that of the hysteroscopy combined with biopsy. This study examined 160 patients who applied to Medipol University Gynaecology and Obstetrics Clinic. The rate of those who have never conceived was 40.6%, 1 pregnancy was 16.3%, 2 pregnancies was 18.8%, nulliparity was most common, no history of abortus was in majority, 2 cases with 1 ectopic pregnancy and 3 cases with 2 ectopic pregnancy histories were detected. The mean double wall thickness of the endometrium was 10.9 ± 3.7 mm. Hysteroscopic evaluation with a biopsy had highest specifity, sensitivity, positive and negative predictive values.

Conclusion: The goal of this study is to evaluate the worth of diagnostic techniques. An examination of the data from our investigation revealed the low sensitivity and specifcity of transvaginal ultrasonography. Hysteroscopy is more accurate in diagnosing and treating submucous fibroids and endometrial polyps than TVUSG. H/S must adhere to TVUSG. The greatest diagnostic outcomes for the evaluation of endometrial diseases come from the combination of hysteroscopy and endometrial D&C. Multicenter research containing more patients is required to contribute more literately.

Keywords: Abnormal uterine bleeding, transvaginal ultrasound, dilatation and curretage, hysteroscopy

Öz

Amaç: Anormal uterin kanamanın (AUB) incelenmesinde transvajinal ultrasonografi (TVUSG) muayenesi, dilatasyon ve küretaj (D&C) yaklaşımı ve histeroskopik değerlendirme sıklıkla kullanılmaktadır. AUB tespiti için özel test histopatolojik değerlendirmedir. Çalışma, AUB'nin ayırıcı tanısı için TVUSG, D&C ve histeroskopinin doğruluğunu kontrol etmeyi amaçladı.

Gereç ve Yöntem: Bu retrospektif çalışmaya TVUSG, D&C veya histeroskopide endometrial patoloji olduğu düşünülen AUB'lu olgular dahil edildi. Retrospektif çalışmamız anormal uterin kanama şikayeti ile kliniğimize başvuran 160 hasta üzerinde yapıldı. Son patolojik tanı referans test olarak kabul edildi ve patolojik tanı ile D&C, histereskopi ve TVUSG'nin duyarlılık ve özgüllüğü kontrol edildi.

Bulgular: Biyopsi ile birlikte histereskopi, histopatolojik değerlendirme ile en yüksek korelasyonu sağladı. Bununla birlikte, TVUSG ile elde edilen istatistiksel değerler, tek başına histereskopi ve D&C ile karşılaştırılabilir, ancak biyopsi ile kombine histeroskopiden daha düşüktü. Bu çalışmada Medipol Üniversitesi Kadın Hastalıkları ve Doğum Kliniği'ne başvuran 160 hasta incelenmiştir. Hiç gebe kalmayanların oranı %40,6, 1 gebelik %16,3, 2 gebelik %18,8, en sık nulliparite, hiç abortus öyküsü çoğunlukta, 2 olgu 1 ektopik gebelik ve 3 olgu 2 ektopik gebelik öyküleri tespit edildi. Endometriyumun ortalama çift duvar kalınlığı 10.9 ± 3.7 mm idi. Biyopsi ile histeroskopik değerlendirme en yüksek özgüllük, duyarlılık, pozitif ve negatif prediktif değerlere sahipti.

Sonuç: Transvajinal ultrason, AUB'ye yol açan endometrial patolojilerin değerlendirilmesinde kolayca bulunabilen ve tekrarlanabilir bir görüntüleme tekniğidir. Ancak TVUSG'nin özgüllüğü oldukça düşüktür. Çalışma popülasyonumuzdaki endometrial patolojileri doğru bir şekilde saptamak için kullanılan yöntemler arasında en yüksek duyarlılık ve özgüllük biyopsi ile birlikte histereskopi ile elde edilmiştir. Yine de TVUSG, tek başına histereskopi ve D&C ile karşılaştırıldığında benzer istatistiksel değerler sağlar. Çalışmamızda amacımız tanısal yöntemlerin değerini belirlemektir. Literatüre katkısı açısından çok merkezli ve daha çok sayıda hastanın yer aldığı araştırmaların yapılması gerekmektedir.

Anahtar Kelimeler: Anormal uterin kanama, transvajinal ultrason, dilatasyon ve küretaj, histereskopi



INTRODUCTION

Changes in the endometrial layer lining the uterine cavity occur due to hormonal and non-hormonal etiologies.^[1] Some of these might be in neoplastic or non-neoplastic origin.^[2] These pathologies appear clinically as abnormal uterine bleeding (AUB). Considering the applications to gynecology outpatient clinics, AUB is a significant problem.

Abnormal uterine bleeding is the general definition of deviations from the normal menstrual cycle pattern and is an important clinical condition that can emerge for different reasons.^[3] A normal menstrual cycle lasts between 28 +/- 7 days (21-45 days for adolescents), of which bleeding occurs in approximately 2-6 days.^[4] The amount of bleeding is on average 20-60 mL/cycle. There might be differences in the menstrual cycle duration in the reproductive period. Abnormal uterine bleedings seen during and after the reproductive period are clinically grouped under 8 headings; oligomenorrhea, polymenorrhea, hypermenorrhea (menorrhagia), hypomenorrhea, metrorrhagia, menometrorrhagia, contact bleeding (Postcoital bleeding, postmenopausal bleeding. The prevalence of anovulatory cycles increases under the age of 20 and above the age of 40. 50% of the applicants with AUB are in the peri-postmenopausal period, 30% are in the reproductive period, and remaining 20% are in the adolescence period.^[2]

FIGO (International Federation of Gynecology and Obstetrics) defined AUB terminology according to the distribution of symptoms in 2011 as heavy menstrual bleeding (HMB), intermenstrual (IMB) bleeding and their combinations.^[5] The causes of AUB were grouped under two groups as uterine structural anomalies and non-structural anomalies. The first group includes pathologies such as polyps, adenomyosis, leiomyoma, hyperplasia and, malignancy while the second group includes coagulopathies, ovarian dysfunction, endometrial, iatrogenic and unclassified anomalies (PALM-COEIN, 3).

The priority in diagnosis is to identify the underlying pathology in order to exclude pregnancy and cancer and to provide appropriate treatment.^[4] The anamnesis should be detailed and include important questions to explain the etiology of bleeding.^[5] Age, pregnancy history, contraception status, last menstruation date, menstrual interval, duration and bleeding pattern, non-menstrual bleeding, other bleeding-related signs (anemia) and symptoms, postcoital bleeding/pain, type of discharge if present, history of trauma, drug intake, chronic stress, body weight changes, systemic diseases are essential for preliminary diagnosis.^[5] After primary anamnesis and physical examination are performed an interventional/noninterventional diagnostic technique is usually required. Transvaginal ultrasonography (TVUSG) is preferred as an easy-to-use, non-invasive imaging method for diagnosis of AUB.^[6] Transvaginal ultrasonography is also useful in detecting uterine and adnexial pathologies.^[6] It is a diagnostic tool that guides the invasive procedures that might be required for a definitive diagnosis. Dilatation and curettage (D&C) is also used to reach the diagnosis by performing endometrial sampling and could

be executed in outpatient clinic conditions.^[7] Hysteroscopy (H/S), on the other hand, is a minimally invasive diagnosis and treatment method that directly evaluates endometrial pathologies and allows visual sampling and/or intervention.^[8] All these techniques could be used alone or in combination to reach a diagnosis. Yet histopathological evaluation is golden standard for final diagnosis. So knowledge of predictive value of each diagnostic method gains importance in choice of diagnostic tool for clinical practitioner. Depending on these; we aimed to evaluate the endometrial pathologies in a group of Turkish patient population with AUB using TVUSG, D&C, and H/S methods, and to compare the predictive value of each technique by comparing their estimation of accurate diagnosis reached by gold standard histopathological evaluation.

MATERIAL AND METHOD

Among the patients who applied to Medipol University Faculty of Medicine, Department of Obstetrics and Gynecology with the complaint of AUB, 160 patients who met criteria were included. A total of 160 patients (aged; 38±7, 21-68 years) included in the study were evaluated with TVUSG, D&C and operative H/S. Ethical approval for study was obtained from the Ethics Committee of Medipol University Non-Invasive Clinical Researches. The study was performed in retrospective manner. Diagnostic methods used during examination and diagnosis were compared with those who were diagnosed with histopathology (with normal results (29 people), endometrial polyp (81 people), endometrial hyperplasia (27 people), leiomyoma (21 people), endometrial cancer (2 people)).

Demographic, radiological and histopathological findings of the patients were obtained from the archive records. The age, gravida and parity history of the patients, the mode of delivery if they gave birth, abortion and ectopic pregnancies were recorded as study data. TVUSG, D&C, and/or H/S evaluation was required as criteria for inclusion. Whether the patients had intrauterine devices, oral contraceptive use, previous gynaecological surgeries and intervention information were noted. Systemic physical examination and gynaecological examination findings of each patient were also recorded.

Transvaginal ultrasonographic evaluation was performed using General Electric Logiq brand ultrasound and 8-11 MHz vaginal probe. Double wall endometrial thickness was measured while the uterus was viewed in the sagittal plane. When uterine sagittal and coronal planes were evaluated, hyperechogenic focal thickenings were defined as endometrial polyps, and lesions with more heterogeneous hypoechogenicity (close to myometrial echogenicity) in the cavity compared to polyps were defined as submucous leiomyoma.

As a H/S instrument, an operative 5 mm rigid hysteroscope from Karl Storz company (Germany) was used. Hysteroscopy was performed under general anesthesia in operating room conditions. After the cervix and vagina

were cleaned with povidone iodine solution while the patients were in the dorsolittotomy position, the uterine cavity was entered with a resectoscope by holding it at 11 o'clock with a single gear and dilating it up to the 9-10 hegar bougie. Cavity distention was achieved with mannitol (resectisol) or 0.9% NaCl (physiological saline) solutions. The appearance of the endometrium, whether it was compatible with the menstrual phase, the presence of pathologies occupying uterine cavity, uterine anomalies and both ostia were recorded. Endometrial polyp was defined as a smooth-surfaced, pedunculated or broad-based soft structure, and submucous leiomyoma was defined as shiny, psoriatic, usually broad-based, hard and vascularized lesions covered by the endometrium. If the endocervical canal, endometrial cavity, and right and left tubal ostia could be evaluated, the procedure was considered adequate and these cases were included in our study. Tissue sampling was done from suspicious areas. These materials were sent to pathology in 10% formaldehyde solution and were evaluated histopathologically. Patients with adhesions in the cavity, intramural myomas displacing the cavity and congenital anomalies were not included in our study. Definitive diagnosis was made according to histopathological results. Sensitivity, specificity, positive and negative predictive values were calculated separately for TVUSG, H/S biopsy and D&C procedures.

Version 21.0 of the SPSS (Statistical Package or the Social Sciences) program (IBM, Armonk, NY, USA) was used for statistical analysis of the data. Descriptive statistics were expressed as mean±standard deviation or median (minimum-maximum) for discrete and continuous numerical variables, and number of cases and (%) for categorical variables. Cross-table statistics were used to compare categorical variables (Chi-square). A p value <0.05 was accepted as threshold for statistical significance.

RESULTS

This study was carried out on 160 cases who applied to Medipol University Gynaecology and Obstetrics Clinic. Obstetric and pregnancy history of patients are presented in **Table 1**. The rate of those who have never conceived (nulligravid) was 40.6% (n:65), 1 pregnancy was 16.3% (n:26), 2 pregnancies was 18.8% (n:30). In means of parity; nulliparity was most common (54.4%, n:87), followed by 2 and 1 parities (18.8%, 11.3%, n: 30, 18 respectively).

Patients with no history of abortus were in majority (76.9%, n:123) followed by 1 and 2 abortions (15%, 3.1%, n:24, 5 respectively). While there was no ectopic pregnancy history in 96.9% (n:155) of our patients, 2 cases with 1 ectopic pregnancy and 3 cases with 2 ectopic pregnancy histories were detected. None of the patients with birth history had both normal vaginal delivery and C-section history, while normal vaginal delivery was more common compared to C-section (n: 54 vs 21 respectively).

Table 1. Demographic features of the study subjects

Age, years	38±7
Menopause, n	0.0812
Gravida, n	1.51 ± 0.35
Parity, n	1.09 ± 0.4
Abortus, n	0.43 ± 0.28
Ectopic pregnancy, n	0.051 ± 0.023
Vaginal delivery rate	0.85 ± 0.019
C-section rate	0.243 ± 0.123
Endometrial thickness, mm	10.9±3.7
Data are presented as mean ± standard deviation	

Transvaginal ultrasonography preliminary diagnosis findings of patients were as follows; normal (34.4%, n:55), endometrial polyp (36.3%, n:55), endometrial hyperplasia (23.1%, n:37), leiomyomatosis (6.3%, n:10). The mean double wall thickness of the endometrium was found to be 10.9±3.7 mm. Hysteroscopic preliminary diagnosis findings of patients were as follows; normal (28.2%, n:46), endometrial polyp (43.1%, n:69), endometrial hyperplasia (19.4%, n:31), leiomyomatosis (8.8%, n:14). Dilatation and curettage preliminary diagnosis findings of patients were as follows; normal (35.6%, n:57), endometrial polyp (38.3%, n:61), endometrial hyperplasia (19.7%, n:30), leiomyomatosis (6%, n:10), endometrial cancer (1.2%, n:10). We also analyzed patients' H/S biopsy results and observed that preliminary diagnosis were as follows; normal (23.1%, n:37), endometrial polyp (50.6%, n:81), endometrial hyperplasia (13.1%, n:21), leiomyomatosis (13.1%, n:21, **Table 2**). Final histopathological findings were as follows; normal (23.1%, n:37), endometrial polyp (50.6%, n:81), endometrial hyperplasia (21%, n:13.1), leiomyomatosis (14.3%, n:23) and endometrial cancer (1.2%, n:2). Crosssectional comparison of each method with histopathological findings are presented in **Table 3**. Specificity, sensitivity, positive and negative predictive values for each diagnostic tool are presented in **Table 4**. Hysteroscopic evaluation with a biopsy had highest specificity, sensitivity, positive and negative predictive values (**Table 4**).

Table 2. Initial diagnosis obtained with several diagnostic methods and the definitive diagnosis provided by histopathological assessment

	Transvaginal Ultrasonography	Hysteroscopy	Hysteroscopy with biopsy	Dilatation and Curettage	Definitive diagnosis with histopathology
Normal	55 (34,4%)	46 (28,8%)	37 (23,1%)	57 (35,6%)	29 (18,1%)
Endometrial polyp	58 (36,3%)	69 (43,1%)	81 (50,6%)	61 (38,3%)	81 (51%)
Endometrial hyperplasia	37(23,1%)	31(19,4%)	21 (13,1%)	30 (18,7%)	27 (16,7%)
Leiomyoma	10 (6,3%)	14(8,8%)	21 (13,1%)	10 (6,0%)	21 (13.1%)
Endometrial Cancer	0,00	0,00	0,00	2 (1.2%)	2 (1.2%)

Table 3: Comparison of TVUSG, H/S and D&C preliminary and histopathological definitive diagnosis

	Histopathological diagnosis				
	Normal	E. polyp	E. hyperplasia	Leiomyom	
TVUSG					
Normal	24	10	16	5	
E. polyp	1	51	3	3	2
E. hyperplasia	4	15	7	9	
Leiomyomatosis	-	5	1	4	
H/S					
Normal	27	1	16	1	
E. polyp	-	66	1	2	2+
E. hyperplasia	2	14	10	4	
Leiomyomatosis	-	-	-	2	
H/S pathology					
Normal	29	-	6	-	
E. polyp	-	81	-	-	
E. hyperplasia	-	-	21	-	
Leiomyomatosis	-	-	-	21	2
E. Cancer	-	-	-	-	
D&C					
Normal	24	22	-	11	-
E. polyp	2	59	-	-	-
E. hyperplasia	-	-	30	-	-
Leiomyomatosis	1	-	-	9	-
E. cancer	-	-	-	-	2

Table 4. Diagnostic accuracy of the different diagnostic techniques (Histopathological results have been accepted as the definitive diagnosis)

	Sensitivity	Specificity	PPV	NPV
TVUSG	82.7%	83.9%	53.3%	95.6%
Hysteroscopy	93.1%	86.2%	60.0%	98.2%
Hysteroscopy with biopsy	100.0%	87.2%	78.0%	100.0%
D&C	88.8%	75.1%	42.1%	97.8%

TVUSG= Transvaginal ultrasonography, D&C= Dilatation and curettage, NPV= Negative predictive value, PPV= Positive predictive value

DISCUSSION

It is known that one third of the patients who apply to gynaecology outpatient clinics present with the complaint of AUB.^[6] Endometrial pathologies are most commonly encountered as AUB in clinical practice. Abnormal uterine bleeding is the second most common complaint of gynaecologists after vaginal infections. When the perimenopausal/ postmenopausal age groups are considered together, AUB constitutes 69% of the complaints requiring gynaecological referral.^[7] The biggest challenge in patients with AUB is to differentiate between those with dysfunctional uterine bleeding who only need medical treatment, and those with organic lesions that will require surgery. Different incidences of anatomical causes of AUB are seen in the literature.

In the literature, benign anatomical pathologies such as polyps, submucous fibroids and endometrial hyperplasia were found in 30-50% of cases in women with AUB, malignant pathologies were found in around 1% of patients under 50 years of age and 10-15% of patients over 50 years of age.^[8] In our study, no correlation of age on endometrial pathologies was observed.

Diagnostic tests often do not provide a 100% definitive diagnosis, but they provide enough information to rule out a

diagnosis possibility and help to identify the tests that are likely to make a definitive diagnosis. Transvaginal ultrasonography is an easy diagnostic technique used in the detection of endometrial pathologies and can be easily applied in outpatient settings. It provides recognition of uterine pathology in the majority of cases in women with postmenopausal bleeding and menstrual irregularities. Therefore, it is used for first-line examination.^[9] However, the specificity of endometrial thickness measurement with TVUSG in premenopausal women is low and it is not suitable for detecting intracavitary abnormalities.^[10] In our study, the sensitivity of TVUSG was calculated as 82.7% and the specificity as 83.9%, which is similar with the current literature.^[10] Transvaginal ultrasonography, which is a non-invasive diagnostic tool in the diagnosis of AUB, can be preferred to techniques such as D&C in detecting endometrial abnormalities. However, TVUSG fails to differentiate endometrial abnormalities such as endometrial polyps, fibroids, and blood clots, and its diagnostic sensitivity is low, varying between 88% and 96%.^[11] In our study, the preliminary diagnosis of polyps by TVUSG was found in 87.9% and is compatible with the literature.

Karlsson et al. has reported that the double-wall endometrial thickness measurement of 20 mm and above, that was performed in 759 endometrial cancer patients, was found to be associated with cancer.^[12] In our study the mean double wall thickness of the endometrium was found to be 10.9±3.7 mm and measurement of 2 cancer cases were less than 20 mm (mean 10 mm). Alborzi et al. reported the sensitivity, specificity, positive and negative predictive values for TVUSG as followed; 72%, 92%, 94%, 65% respectively. In a metaanalysis that included 19 prospective studies, it was reported that the accuracy of TVUSG in detecting endometrial lesions was compared with the histopathological results obtained after hysteroscopy and hysterectomy, with a sensitivity between 46% and 100% and a specificity between 12% and 100%.^[13] In our study, the sensitivity, specificity, PPD and NPV calculated for the preliminary diagnosis of TVUSG were found to be 82.7%, 83.9%, 53.3% and 95.6%, respectively. It seems to be compatible with the previous studies. The variability in these obtained values may be due to the TVUSG experience of the practitioners, their interpretation of the observed lesions, the number and diversity of cases, and the difference in reference tests. In addition, the patient's menstruation or menopausal status is one of the most important reasons for this difference. The fact that the endometrial thickness varies as a result of hormonal effects that differ according to the phases of the cycle in menstruating patients might cause small lesions not to be visualized in the thickening endometrium or a thick endometrium might feel like a lesion on its own and cause misinterpretations. This may be the most important reason for the difference in sensitivity and specificity of TVUSG reported in the literature.^[14] In a study previous carried by Emanuel et al. stated that TVUSG and H/S combined and supported with histological evaluation, is the most appropriate reference technique for the evaluation of endometrial pathologies.^[15]

Benign anatomical pathologies such as polyps, submucous fibroids and endometrial hyperplasia were found in 30-50% of cases in women with AUB while malignant pathologies were found in 1% of patients under 50 years of age and 10-15% of patients over 50 years of age.^[16] In our study, no evaluation was made according to age difference. The limited number of cases and the low number of malignancies may be considered as a limiting factor.

Hysteroscopy enables gynaecologist to visualize the endometrial cavity for any endometrial or endocervical pathology. In modern obstetrics and gynaecology, instead of blindly performing D&C or endometrial biopsy, targeted biopsy with H/S, to investigate possible intrauterine disease, or the endometrial cavity, is a commonly preferred method. Hysteroscopy is considered as a "gold standard" technique for the evaluation of the uterine cavity and the detection of intrauterine pathologies.^[17]

Lo et al. reported that H/S results without biopsy for endometrial carcinoma and hyperplasia have low sensitivity for diagnostic value. The authors stated that the combination of H/S with biopsy would increase the accuracy of the results.^[18] The combined use of H/S and endometrial biopsy can give 100% accurate results in early diagnosis.^[19] In our study, it was seen that it has 100% diagnostic value in those who underwent hysteroscopic biopsy. Gimpelson and Rappold suggested that H/S may be superior to D&C in the diagnosis of pathological conditions within the uterine cavity.^[20] In the results obtained in our study, it was revealed that visual material removal with hysteroscopy is superior to dilatation and curettage, where the lesion is removed without being seen. The specificity and positive predictive value of hysteroscopy in cases with AUB has been found close to 100% in some studies. Compared to D&C alone, especially endometrial polyps and submucous fibroids can be recognized with greater precision.^[21] We made the same evaluation with the results obtained from our study. Many studies have reported that H/S is more valuable than D&C in the diagnosis of AUB.^[22] Although submucous fibroids and polyps, especially those close to the fundus and cornu, cannot be diagnosed during curettage, they are easy to diagnose with H/S. Classical D&C fails to detect 25% of lesions on the endometrial surface.^[23] According to the data of our study, this rate has emerged as 25% difference for polyps and close to 100% for fibroids. Gimpelson et al. reported that H/S and direct biopsy for endometrial pathologies were more successful than D&C procedures.^[24] In our study, hysteroscopic diagnosis rates of polyps and fibroids were 50.6% and 13.1%, respectively, while these rates were 38.3% and 6% with dilatation and curettage.

Endometrial polyps were detected in 81 of 160 patients included in our study. 22 of these cases could not be detected by D&C so we can propose that D&C alone may not be an ideal diagnostic tool for the diagnosis of AUB. The sample taken may be insufficient, and 10 to 35% of endometrial lesions may not be accurately diagnosed.^[25] In our study, this

rate was found to be 27%. Madan et al reported that H/S was more sensitive than D&C in recognizing endometrial polyps and submucous fibroids, but less sensitive in recognizing endometrial hyperplasia and endometrial carcinomas.^[26] In our study we also observed findings consistent with this study. The sensitivity, specificity, PPD and NPD values of H/S pathology results were found to be 100%, 87.2%, 78% and 100%, respectively, D&C values were inferior to these results. We observed that H/S was superior to D&C for diagnosis of polyps and submucous myomas.

In our study, the sensitivity of TVUSG in diagnosing endometrial polyps was 87.9% and specificity 83.9%. On the other hand, we observed that the sensitivity and specificity of H/S alone were 93.1% and 86.2% respectively while H/S combined with tissue sampling had 100% and 87.2% for same parameters respectively (**Table 4**). Salim et al. evaluated the performance of TVUSG, sonohysterography (SHG), and H/S for diagnosis of endometrial polyps in a group of 5000 patients. They reported the sensitivity of each tool as; 91%, 95%, 90% and the specificity of each tool as; 90%, 92%, and 93%, respectively. The advantage of SHG over H/S is that it can show adnexial masses and intramural components of leiomyomas.^[27] Kilinc et al. compared TVUSG and H/S for the evaluation of endometrial pathologies in a group of 116 patients. They reported sensitivity and specificity for each method as 78.26%-51.35% and 85.51% - 67.57%, respectively.^[28]

Endometrial hyperplasia is the proliferation of endometrial glands in irregular shape and size. It is an atypical cellular increase in the ratio of gland-stroma compared to the normal proliferative endometrium. It occurs as a result of dysregulation in estrogen/progesterone balance.^[29] In a study evaluating the risk of endometrial cancer in women with endometrial hyperplasia with and without atypia, authors reported increased risk in patients with cellular atypia (28% vs 5%).^[30] Most women with endometrial hyperplasia with atypia might also have endometrial cancer at the same time.^[31] In a study of 2572 patients, endometrial cancer with atypia was also found in the hysterectomy results of 37% of the patients whose endometrial biopsies had a result of endometrial hyperplasia with atypia alone.^[32] Therefore, the diagnosis of endometrial hyperplasia, which is a premalignant lesion, is very important for clinical practice. In our study, endometrial hyperplasia was reported with a rate of 16.7% in 27 cases according to the histopathological definitive diagnosis. Endometrial hyperplasia was detected in 16 of 55 cases who were preliminary diagnosed with normal endometrium in TVUSG. Endometrial hyperplasia was detected in 16.2% of 37 cases whose biopsy results were reported as normal H/S.

In the literature, the incidence of submucous myoma has been reported to be 6-10%.^[33] Uterine leiomyomas (fibroids) are the most common pelvic tumor in women. Submucous leiomyomas are an important cause of AUB and might cause anemia.^[34] In our study, 13% submucous myoma was detected

in 21 cases according to the histopathological definitive diagnosis. Submucous leiomyoma detected as a result of a combination of H/S and biopsy was found in 11 (19.3%) of the biopsy results reported as normal by D&C. Hysteroscopy seems superior to D&C in detecting intracavitary uterine lesions. D&C is also considered superior to H/S-guided biopsy in the detection of cancer and diagnosis of endometrial hyperplasia

CONCLUSION

This study's objective is to assess the value of diagnostic methods. Transvaginal ultrasonography has low sensitivity and specificity, according to an analysis of the data from our study. In cases of submucous fibroids and endometrial polyps, hysteroscopy performs diagnostic and therapeutic tasks more accurately than TVUSG. H/S ought to follow TVUSG. The combination of hysteroscopy and endometrial D&C yields the best diagnostic results for the assessment of endometrial pathologies. To make a greater literary contribution, multicenter studies involving more patients are necessary.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Medipol University Ethics Committee (Date: 10/08/2017, Decision No: 10840098-604.01.01-E26932).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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REFERENCES

- Deligdisch L. Hormonal pathology of the endometrium. *Mod Pathol*. 2000 Mar;13(3):285-94.
- Stenbäck F, Väänänen R, Kauppila A. Surface ultrastructure of human endometrium. Effect of hormonal status and neoplastic progression. *Eur J Obstet Gynecol Reprod Biol*. 1980 Oct;11(2):69-84.
- Committee on Practice Bulletins—Gynecology. Practice bulletin no. 128: diagnosis of abnormal uterine bleeding in reproductive-aged women. *Obstet Gynecol* 2012;120:197.
- Edelman A, Micks E, Gallo MF, Jensen JT, Grimes DA. Continuous or extended cycle vs. cyclic use of combined hormonal contraceptives for contraception. *Cochrane Database Syst Rev*. 2014 Jul 29;2014(7):CD004695.
- Davis E, Spazak PB. Abnormal Uterine Bleeding. 2022 Sep 9. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023.
- McFarlin BL. Ultrasound assessment of the endometrium for irregular vaginal bleeding. *J Midwifery Womens Health*. 2006;51(6):440-9.
- Abdelazim IA, Abdelrazak KM, Elbiaa AA, Al-Kadi M, Yehia AH. Accuracy of endometrial sampling compared to conventional dilatation and curettage in women with abnormal uterine bleeding. *Arch Gynecol Obstet*. 2015;291(5):1121-6.
- Tsonis O, Gkrozou F, Dimitriou E, Paschopoulos M. Comparative retrospective study on transvaginal sonography versus office hysteroscopy in the diagnosis of endometrial pathology among different subgroups. *J Obstet Gynaecol Res*. 2021;47(2):669-78.
- Kjerulff KH, Erickson BA, Langenberg PW. Chronic gynecological conditions reported by US women: findings from the National Health Interview Survey, 1984 to 1992. *Am J Public Health* 1996;86:195.
- Munro MG, Critchley HO, Broder MS, et al. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. *Int J Gynaecol Obstet* 2011;113:3.
- Bayer SR, DeCherney AH. Clinical manifestations and treatment of dysfunctional uterine bleeding. *JAMA*. 1993;269(14):1823-8.
- Demers C, Derzko C, David M, et al. Gynaecological and obstetric management of women with inherited bleeding disorders. *Int J Gynaecol Obstet*. 2006. 95(1):75-87.
- Spencer CP, Whitehead MI. Endometrial assessment re-visited. *Br J Obstet Gynaecol* 1999;106:623
- Motashaw ND, Dave S. Diagnostic and therapeutic hysteroscopy in the management of abnormal uterine bleeding. *J Reprod Med*. 1990 Jun;35(6):616-20.
- Mencaglia L, Perino MD. Diagnostic hysteroscopy today. *Acta Eur Fertil*. 1986;17:431-9.
- Cacciatore B, Ramsay T, Lehotvirta P, et al. Transvaginal Sonography and hysteroscopy in postmenopausal bleeding. *Acta Obstet Gynecol Scand* 1994;73:413-6.
- Dijkhuizen FP, Brolmann HA, Potters AE, et al. The accuracy of transvaginal ultrasonography in the diagnosis of endometrial abnormalities. *Obstet Gynecol*. 1996;87:345-9.
- O'Connell LP, Fries MH, Zeringue E, et al. Triage of abnormal postmenopausal bleeding: a comparison of endometrial biopsy and transvaginal sonohysterography versus fractional curettage with hysteroscopy. *Am J Obstet Gynecol* 1998;178:956-61.
- Karlsson B, Granberg S, Wikland M, et al. Transvaginal ultrasonography of the endometrium in women with postmenopausal bleeding: a Nordic multicenter study. *Am J Obstet Gynecol*. 1995;172:1488-94
- Farquhar C, Ekeroma A, Furness S, et al. Systematic review of transvaginal ultrasonography, sonohysterography and hysteroscopy for the investigation of abnormal uterine bleeding in premenopausal women. *Acta Obstet Gynecol Scand*. 2003;82:493-504.
- Feng L, Dingheng L. Evaluation of inrauterine disorders by hysteroscopy and transvaginal sonography. *Gynaecological endoscopy* 2002;11:401-4
- Mark H. Emanuel, Marion J. Verdel, Kees Wamsteker, et al. A prospective comparison of transvaginal ultrasonography and diagnostic hysteroscopy in the evaluation of patients with abnormal uterine bleeding: clinical implications. *Am J Obstet Gynecol*. 1995;172(2 Pt 1):547-52.
- Mencaglia L, Perino MD. Diagnostic hysteroscopy today. *Acta Eur Fertil*. 1986;17:431-9.
- Philip G. In the management of abnormal uterine bleeding is Office hysteroscopy preferable to ultrasonography *Journal of Minimal Invasive Gynecology* 2007,14;1:12-14
- Lo KW, Yuen PM. The role of outpatient diagnostic hysteroscopy in identifying anatomic pathology and histopathology in the endometrial cavity. *J Am Assoc Gynecol Laparosc*. 2000;7(3):381-5.
- Hamou J. E. Hysteroscopy and microcolposcopy. *Text and Atlas* P. 99-113 1991.
- Gimpelson RJ, Rappold HO. A comparative study between panoramic hysteroscopy with directed biopsies and dilatation and curettage. A review of 276 cases. *Am J Obstet Gynecol*. 1988;158 (3 Pt 1).
- Goldstein SR, Zeltser I, Horan CK, et al. Ultrasonography-based triage for perimenopausal patients with abnormal uterine bleeding. *Am J Obstet Gynecol*. 1997;177:102-8.

29. Yücesoy Ğ. Görge H: Prekanseröz ve kanseröz endometriyum lezyonlarında histeroskopinin diagnostik değeri. *Jinekoloji Obstetrik Derg* 1994;8:17-21.
30. de Jong P, Doel F, Falconer A. Outpatient diagnostic hysteroscopy. *Br J Obstet Gynaecol*. 1990;97 (4):299-303.
31. Gimpelson RJ, Rappold HO. A comparative study between panoramic hysteroscopy with directed biopsies and dilatation and curettage. A review of 276 cases. *Am J Obstet Gynecol* 1988;158:489-92.
32. Parasnis, H.B., Parulaker, S.U.: Significance of negative hysteroscopic view in abnormal uterine bleeding. *J Postgrad Med*. 38:62-64, 1992.
33. Madan SM, Al-Jufairi ZA. Abnormal uterine bleeding. Diagnostic value of hysteroscopy. *Saudi Med J*. 2001;22 (2):153-6.
34. Salim S, Won H, Nesbitt-Hawes E. Diagnosis and management of endometrial polyps: a critical review of the literature. *J Minim Invasive Gynecol* 2011;18:569
35. Kılınç H, Cengiz H, Kaya C, et al. Endometrial Patolojilerin Değerlendirilmesinde Transvajinal Ultrasonografi ile Ofis Histeroskopinin Karşılaştırılması. *Yeni Tıp Derg* 2012;298 (1) :23-26.
36. Hedrick Ellenson L, Ronnett BM, Kurman RJ. Precursor Lesions of Endometrial Carcinoma. In: Blaustein's Pathology of the Female Genital Tract, 6th ed, Kurman RJ, Hedrick Ellenson L, Ronnett, BM. (Eds), Springer, New York 2010. p.360-361
37. Lacey JV Jr, Sherman ME, Rush BB. Absolute risk of endometrial carcinoma during 20-year follow-up among women with endometrial hyperplasia. *J Clin Oncol* 2010;28:788.
38. Trimble CL, Kauderer J, Zaino R. Concurrent endometrial carcinoma in women with a biopsy diagnosis of atypical endometrial hyperplasia: a Gynecologic Oncology Group study. *Cancer* 2006;106:812
39. Rakha E, Wong SC, Soomro I. Clinical outcome of atypical endometrial hyperplasia diagnosed on an endometrial biopsy: institutional experience and review of literature. *Am J Surg Pathol* 2012;36:1683
40. Di Spiezo Sardo A, Mazzon I, Bramante S, et al. Hysteroscopic myomectomy: a comprehensive review of surgical techniques. *Hum Reprod Update*. 2008;14(2):101-19.
41. Puri K, Famuyide AO, Erwin PJ. Submucosal fibroids and the relation to heavy menstrual bleeding and anemia. *Am J Obstet Gynecol* 2014;210:38.e1.