

Clinical Bleeding Patterns Improve Risk Stratification Beyond Endometrial Thickness for Detecting Endometrial Polyps in Reproductive-Aged Women

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ABSTRACT

Endometrial polyps are a common structural cause of abnormal uterine bleeding (AUB) in reproductive-aged women. However, managing cases with equivocal ultrasound findings remains a clinical challenge. This prospective study evaluated whether clinical bleeding characteristics, combined with endometrial thickness measured by transvaginal ultrasonography, improve risk stratification for difficult-to-diagnose endometrial polyps.

This prospective observational study included 1,073 reproductive-aged women presenting with AUB who underwent endometrial sampling. To focus on diagnostically challenging cases, patients with unequivocally identified intrauterine space-occupying lesions on ultrasonography were excluded. Based on histopathology, patients were classified as having an endometrial polyp (n=453) or benign endometrium (n=620). Clinical characteristics, bleeding patterns, oral contraceptive (OCP) use, and ultrasonographic findings were recorded. Multivariable logistic regression adjusted for age, BMI, parity, and cycle phase identified independent variables associated with polyps. ROC analysis assessed diagnostic performance.

Endometrial thickness was higher in patients with polyps (10.56 ± 4.63 vs 9.28 ± 4.00 mm, $p < 0.001$) and remained an independent predictor (OR 1.071, 95% CI 1.038–1.106, $p < 0.001$). Premenstrual bleeding showed a strong positive association (OR 3.572, $p < 0.001$), whereas postmenstrual bleeding (OR 0.506, $p < 0.001$) and OCP use (OR 0.757, $p = 0.045$) were inversely associated. Endometrial thickness alone demonstrated limited performance (AUC=0.582). However, the combined multivariable clinical model yielded fair discrimination (AUC=0.686) with higher specificity (77.4%).

Endometrial thickness and specific bleeding patterns are independent variables associated with endometrial polyps. While the standalone diagnostic value of ultrasound is limited in equivocal cases, integrating clinical bleeding characteristics improves risk stratification to guide clinical decisions.

Keywords: Abnormal Uterine Bleeding, Endometrial Polyps, Endometrial Thickness, Transvaginal Ultrasonography, Endometrial Sampling

Introduction

Abnormal uterine bleeding (AUB) is one of the most common gynecological complaints among reproductive-aged women and represents a major reason for outpatient gynecologic consultations worldwide. The International Federation of Gynecology and Obstetrics (FIGO) classifies the causes of AUB using the PALM–COEIN system, which distinguishes structural causes such as endometrial polyps from non-structural etiologies (1). Clinically, polyps may present with a wide spectrum of bleeding patterns, including

intermenstrual bleeding, menorrhagia, postmenstrual spotting, and prolonged menstrual bleeding (2). Transvaginal ultrasonography (TVUS) is widely accepted as the first-line imaging modality in the evaluation of AUB due to its accessibility, non-invasive nature, and relatively high diagnostic accuracy (3). Among ultrasonographic parameters, endometrial thickness (ET) is frequently used as a surrogate marker of endometrial pathology. However, the diagnostic performance of ET alone remains controversial, particularly in reproductive-aged

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women where endometrial thickness varies substantially throughout the menstrual cycle (4).

While obvious intrauterine space-occupying lesions are readily identified via TVUS, previous studies have suggested that ultrasonography alone may have limited sensitivity for detecting focal intrauterine lesions such as endometrial polyps in certain cases (5). The major diagnostic dilemma lies in patients with equivocal or homogeneous endometrial appearances such as a thickened but symmetrical endometrium, an indistinct endometrial-myometrial junction, or the presence of small cystic spaces without a clear polypoid outline where relying solely on standalone ultrasound measurements carries a risk of missing subtle pathologies. Although definitive diagnosis can be achieved through advanced modalities, performing resource-intensive and invasive procedures as first-line screening for all suspected cases is neither ethically justified nor practically feasible. Consequently, increasing attention has been directed toward identifying clinical predictors such as specific bleeding patterns that may improve the detection of structural uterine pathologies (6,7). Recent studies emphasize that integrating these clinical findings with imaging parameters may improve diagnostic accuracy and help guide decisions regarding further invasive procedures (8).

Despite these advances, evidence regarding the combined evaluation of patient-specific bleeding characteristics and ET in reproductive-aged women remains limited, as many studies focus on unselected cohorts that include obvious pathologies. Therefore, the present prospective study aimed to evaluate whether clinical bleeding characteristics, combined with ET measured by TVUS, improve risk stratification for endometrial polyps. By focusing on patients with equivocal ultrasound findings, we sought to develop a practical triage tool to identify women who truly warrant referral for further invasive evaluation.

Materials and Methods

Study design and study population: This prospective observational study was derived from a clinical thesis project. The study was conducted between June 2024 and June 2025 at the Department of Obstetrics and Gynecology, Bagcilar Training and Research Hospital, and ethical approval was granted by the Clinical Research Ethics Committee of Bakirkoy Dr. Sadi Konuk Training and Research Hospital (Approval No: 2024-01-13; Date: May 13, 2024). The study

was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants.

Reproductive-aged women presenting with abnormal uterine bleeding (AUB) who underwent endometrial biopsy following clinical evaluation were prospectively included. Women who were postmenopausal, pregnant, or had known gynecological malignancy or dysplasia were excluded.

Furthermore, patients with unequivocally identified or suspected space-occupying intrauterine lesions on initial transvaginal ultrasonography were deliberately excluded. The rationale for this exclusion is that patients with obvious polypoid lesions already follow a clear clinical pathway (e.g., direct referral for diagnostic or operative hysteroscopy) and do not require a secondary risk stratification model. Our focus was strictly on the clinical 'gray zone'—patients with homogeneous or equivocal endometrial appearances where the diagnosis is challenging, yet the clinical suspicion of an underlying focal lesion remains. In such ambiguous cases, identifying subtle clinical predictors is highly valuable to justify the decision for further invasive testing or referral.

For the purpose of this study, only patients with histologically confirmed endometrial polyp or benign non-polyp endometrium were included. Initially, a total of 1,076 reproductive-aged women were clinically evaluated. Patients with a histopathological diagnosis of malignancy or premalignancy were deliberately excluded to maintain a homogeneous sample for benign focal lesion prediction. Specifically, 3 cases (0.28%) of endometrial malignancy were identified during the study period and were excluded. The final study population consisted of 1,073 women, including 453 patients with endometrial polyps and 620 patients with benign endometrial findings.

Clinical and ultrasonographic evaluation: Demographic and clinical data were recorded prospectively prior to the biopsy procedure. These data included age, body mass index (BMI) categories, parity status, smoking status, oral contraceptive (OCP) use, systemic comorbidities, and reproductive history. Detailed menstrual characteristics and clinical bleeding patterns were also systematically documented, encompassing cycle regularity, intermenstrual bleeding, premenstrual bleeding, postmenstrual bleeding, heavy menstrual bleeding, and the overall duration of symptoms. Heavy menstrual bleeding was defined according to FIGO guidelines as excessive

menstrual blood loss interfering with the woman's physical, emotional, or social quality of life. An 'unclear bleeding pattern' referred to irregular bleeding episodes that did not strictly fit into predefined clinical categories. Symptoms were classified as 'chronic' if they persisted for at least 3 months. OCP use was defined as current regular use for either contraception or medical management of AUB.

All participants underwent a standardized clinical evaluation and transvaginal ultrasonography by the same experienced physician (O.F.B.) to minimize interobserver variability. Ultrasonographic examinations were performed using a Samsung HS50 ultrasound system equipped with a 7-MHz vaginal probe. During the examination, endometrial thickness was measured as the maximum double-layer thickness in the mid-sagittal plane. In cases where intracavitary fluid was present, the fluid was excluded from the measurement. Scans were optimally performed during the bleeding-free interval or when active bleeding was minimal. The current menstrual cycle phase and any additional ultrasonographic findings were meticulously recorded.

Histopathological evaluation and study groups: Endometrial samples were obtained via endometrial biopsy and evaluated histopathologically. Based on pathology results, patients were categorized into two groups:

- Polyp group: histologically confirmed endometrial polyps
- Non-polyp group: benign endometrial findings (proliferative or secretory endometrium)

Patients with other histopathological diagnoses were excluded from the comparative analysis.

Endometrial Sampling Technique: Endometrial biopsies were not performed universally for all patients presenting with AUB. Instead, the decision to perform an endometrial biopsy was strictly based on current clinical guidelines, such as age criteria (e.g., >45 years) or the presence of risk factors for endometrial pathology in younger women (e.g., obesity, chronic anovulation, or failure of medical management). Endometrial samples were obtained in an outpatient clinic setting using either a Pipelle or a Karman cannula, depending on clinical preference and cervical os patency. The operators performing the biopsies were not blinded to the patients' clinical symptoms or ultrasonographic findings, reflecting a pragmatic, real-world clinical setting.

Statistical Analysis: Statistical analyses were performed using IBM SPSS Statistics software (version 20.0; IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean $\pm$ standard deviation (SD) or median (minimum–maximum), while categorical variables were presented as number (n) and percentage (%). The Shapiro–Wilk test was used to assess normality.

Comparisons between groups were performed using the Mann–Whitney U test for continuous variables and the Chi-square or Fisher's exact test for categorical variables, as appropriate.

To identify independent predictors of endometrial polyps, multivariable logistic regression analysis was performed. Multivariable models were additionally adjusted for age, BMI, parity, and menstrual cycle phase (secretory vs. proliferative) to minimize potential confounding and improve the robustness of the analysis. Variables that were clinically relevant or statistically significant in univariable analyses were included in the regression model. Results were reported as odds ratios (ORs) with 95% confidence intervals (CIs).

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of endometrial thickness and the combined clinical prediction model. The area under the curve (AUC) was calculated, and optimal cut-off values were determined using the Youden index, with corresponding sensitivity and specificity values reported. The DeLong test was utilized to compare the differences between the areas under the ROC curves (AUCs) of the models.

A two-sided p-value < 0.05 was considered statistically significant.

Results

A total of 1,073 reproductive-aged women with abnormal uterine bleeding were included in the study. Histopathological examination revealed endometrial polyps in 453 patients (42.2%), whereas 620 patients (57.8%) had benign endometrium (proliferative or secretory phase).

Women with endometrial polyps had significantly greater endometrial thickness than those with benign endometrium (10.56 ± 4.63 mm vs. 9.28 ± 4.00 mm, $p < 0.001$). Premenstrual bleeding was more frequently observed in the polyp group (28.3% vs. 9.0%, $p < 0.001$), whereas postmenstrual bleeding was more common among women with benign pathology (26.0% vs. 11.5%, $p < 0.001$). Chronic symptoms were also more

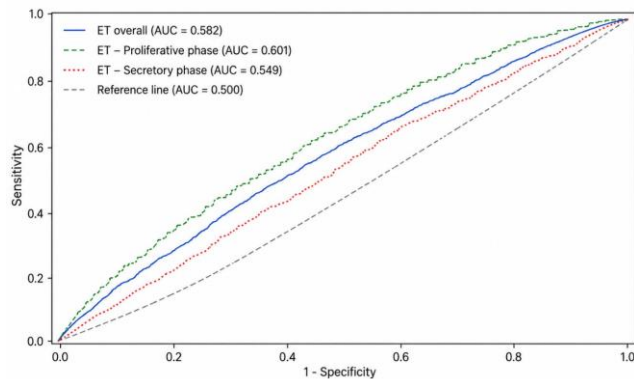


Fig. 1. ROC curves of endometrial thickness (ET) for predicting endometrial polyps. Predictive values are shown for the overall cohort (solid blue line, AUC = 0.582), proliferative phase (dashed green line, AUC = 0.601), and secretory phase (dotted red line, AUC = 0.549)

prevalent in patients with polyps (58.9% vs. 51.5%, $p = 0.016$). No significant differences were observed between the groups regarding age, parity, menstrual cycle phase, body mass index category, menstrual irregularity, diabetes, hypertension, or smoking status (all $p > 0.05$) (Table 1).

Multivariable logistic regression analysis identified endometrial thickness as an independent predictor of endometrial polyps after adjustment for menstrual cycle phase and clinical variables (OR 1.071, 95% CI 1.038–1.106, $p < 0.001$). Premenstrual bleeding demonstrated the strongest positive association with polyp pathology (OR 3.572, 95% CI 2.495–5.113, $p < 0.001$), whereas postmenstrual bleeding was independently associated with a lower likelihood of endometrial polyps (OR 0.506, 95% CI 0.354–0.723, $p < 0.001$). Chronic symptoms remained a significant positive predictor (OR 1.354, 95% CI 1.044–1.755, $p = 0.022$). Notably, although OCP use showed borderline significance in the univariable analysis ($p = 0.060$), it emerged as a significant protective factor in the multivariable model after adjustment for confounders, being associated with reduced odds of polyp detection (OR 0.757, 95% CI 0.576–0.993, $p = 0.045$). Menstrual cycle phase was not independently associated with polyp pathology (OR 0.913, 95% CI 0.695–1.199, $p = 0.511$), and heavy bleeding did not retain statistical significance in the adjusted model (OR 1.238, 95% CI 0.952–1.610, $p = 0.111$) (Table 2).

Receiver operating characteristic (ROC) analysis demonstrated limited discriminatory performance for endometrial thickness alone, with an AUC of 0.582. The optimal overall cut-off value was 9.0

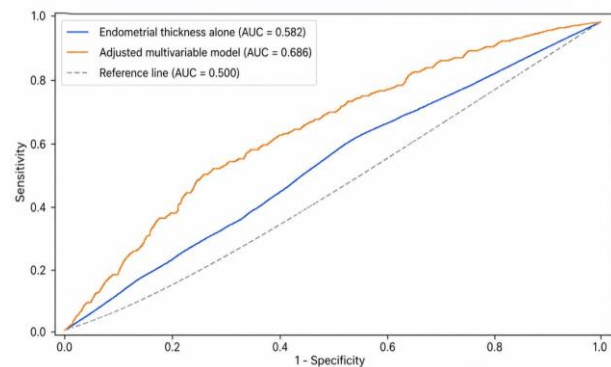


Fig. 2. ROC curves comparing the diagnostic performance of endometrial thickness alone with the adjusted multivariable model. Predictive values are shown for endometrial thickness alone (solid blue line, AUC = 0.582) and the adjusted multivariable model (solid orange line, AUC = 0.686)

mm, providing 61.1% sensitivity and 53.2% specificity. When stratified according to menstrual cycle phase, the discriminatory performance of endometrial thickness remained modest, with AUC values of 0.601 and 0.549 in the proliferative and secretory phases, respectively (Table 3, Figure 1). The addition of menstrual cycle phase did not materially alter the predictive performance of endometrial thickness.

The adjusted multivariable model, incorporating endometrial thickness, menstrual cycle phase, premenstrual bleeding, postmenstrual bleeding, heavy bleeding, chronic symptoms, and OCP use, demonstrated a statistically significant improvement in discriminative performance compared with endometrial thickness alone (AUC 0.686 vs. 0.582; DeLong test, $p < 0.05$). Although sensitivity decreased slightly (52.1%), specificity increased substantially (77.4%), resulting in a significantly enhanced overall discriminative capacity (Table 3, Figure 2).

Discussion

In this prospective study, we evaluated whether clinical bleeding characteristics, in combination with endometrial thickness (ET) measured by transvaginal ultrasonography, improve risk stratification for endometrial polyps in reproductive-aged women presenting with abnormal uterine bleeding (AUB). While transvaginal ultrasonography is the standard first-line imaging modality, its diagnostic accuracy significantly decreases in cases with homogeneous or equivocal endometrial appearances. Our findings demonstrate that although ET is independently associated with polyp detection, its

Table 1: The Demographic and Clinical Characteristics of the Study Population

Variable	Polyp (n=453)	Benign (n=620)	p value
Age	43.84 ± 4.51	43.75 ± 4.61	0.664
Endometrial thickness (mm)	10.56 ± 4.63	9.28 ± 4.00	<0.001
Secretory phase	215/453 (47.5%)	273/620 (44.0%)	0.291
OCP use	143/453 (31.6%)	231/620 (37.3%)	0.060
Multiparity	436/453 (96.2%)	599/620 (96.6%)	0.742
BMI category	N:24.2%, OW:41.7%, Ob:34.1%	N:23.3%, OW:42.2%, Ob:34.6%	0.942
Menstrual irregularity	165/453 (36.4%)	244/620 (39.4%)	0.340
Intermenstrual bleeding	224/453 (49.4%)	284/620 (45.8%)	0.240
Premenstrual bleeding	128/453 (28.3%)	56/620 (9.0%)	<0.001
Postmenstrual bleeding	52/453 (11.5%)	161/620 (26.0%)	<0.001
Unclear bleeding pattern	43/453 (9.5%)	67/620 (10.8%)	0.541
Prolonged bleeding	150/453 (33.1%)	185/620 (29.8%)	0.258
Heavy bleeding	222/453 (49.0%)	266/620 (42.9%)	0.054
Chronic symptoms	267/453 (58.9%)	319/620 (51.5%)	0.016
Diabetes	42/453 (9.3%)	69/620 (11.1%)	0.361
Hypertension	72/453 (15.9%)	106/620 (17.1%)	0.619
Smoking	88/453 (19.4%)	113/620 (18.2%)	0.635

BMI category is summarized as normal / overweight / obese due to source file structure

standalone diagnostic performance is limited. Crucially, integrating specific bleeding patterns—particularly premenstrual bleeding—provides incremental predictive value and enhances the clinical utility of ultrasonographic assessment in these difficult-to-diagnose cases. A major strength of this study lies in its prospective design and large, well-characterized cohort (n = 1,073). By deliberately excluding patients with overt intrauterine lesions on ultrasonography, we specifically focused on a diagnostically challenging clinical 'gray zone' where a triage model is most needed. This approach enabled a more precise

evaluation of subtle determinants of endometrial polyps that might otherwise be overshadowed by obvious pathologies.

ET remains a widely used surrogate marker of intrauterine pathology. In our cohort, increasing ET was independently associated with the presence of endometrial polyps; however, its discriminatory ability was modest (AUC = 0.582). This finding is highly consistent with recent literature (4,5). For instance, Karaosmanoğlu et al. similarly reported limited diagnostic accuracy for transvaginal sonography alone (AUC = 0.566) in detecting endometrial polyps prior to in vitro

Table 2: Multivariable Logistic Regression Analysis

Variable	OR	95% CI	p value
Endometrial thickness (per 1 mm)	1.071	1.038–1.106	<0.001
Menstrual cycle phase (Secretory vs. Proliferative)	0.913	0.695–1.199	0.511
Premenstrual bleeding	3.572	2.495–5.113	<0.001
Postmenstrual bleeding	0.506	0.354–0.723	<0.001
Heavy bleeding	1.238	0.952–1.610	0.111
Chronic symptoms	1.354	1.044–1.755	0.022
OCP use	0.757	0.576–0.993	0.045

Table 3: ROC Analysis of Endometrial Thickness and Adjusted Multivariable Model

Analysis	AUC	Cut-off	Sensitivity (%)	Specificity (%)
ET overall	0.582	9.0 mm	61.1	53.2
ET – Proliferative phase	0.601	9.0 mm	49.6	67.7
ET – Secretory phase	0.549	10.0 mm	65.6	44.0
Adjusted multivariable model	0.686	0.40	52.1	77.4

fertilization (9). This parallel reinforces the premise that relying solely on isolated ultrasonographic parameters is insufficient for definitive diagnosis, highlighting the necessity of our multivariable risk stratification approach.

When analyzing clinical predictors, premenstrual bleeding emerged as the strongest independent variable associated with polyps, yielding an odds ratio (OR) of 3.572. Interestingly, classic predictors like heavy menstrual bleeding did not retain statistical significance in our adjusted model. This contrasts with broader foundational literature, such as the comprehensive reviews by Nijkang et al. (6) and Clark and Stevenson (7), which emphasize heavy or intermenstrual bleeding as the primary clinical hallmarks of polyps, traditionally exhibiting strong predictive associations in unselected populations. The discrepancy between our findings and the classic AUB-P symptomatology described in the literature can be largely attributed to our stringent study design. Because we excluded patients with unequivocally identified ultrasound lesions—who typically present with more severe and classic symptoms—our cohort was strictly restricted to difficult-to-diagnose cases. In such a restricted cohort, the predictive power of classic symptoms

is naturally more modest, whereas subtle patterns like premenstrual spotting become critical clinical indicators of underlying focal pathology.

Regarding patient demographics, although obesity is a well-known classic risk factor for endometrial pathology, we observed similar and relatively high obesity rates in both the polyp and benign groups (34.1% vs. 34.6%, respectively). This lack of difference can be explained by the fact that our entire cohort comprised symptomatic AUB patients, a population in which the baseline prevalence of obesity is inherently elevated across the board. Alongside these baseline characteristics, we also observed an inverse association between oral contraceptive use and endometrial polyps (OR 0.757), which aligns with the known antiproliferative effects of progestins on the endometrium (8). Furthermore, different bleeding phenotypes appear to correspond to distinct pathophysiological mechanisms, as evidenced by the inverse association of postmenstrual bleeding with polyp detection. Menstrual cycle phase also influenced ultrasonographic performance, with slightly better discrimination observed in the proliferative phase, likely due to improved visualization of focal lesions in a thinner endometrium (4,10).

From a clinical perspective, the combined multivariable model (AUC = 0.686) provides a pragmatic risk stratification framework rather than absolute diagnostic certainty. In daily practice, this translates to identifying 'red flags' in patients with equivocal ultrasound images. When a clinician encounters a homogeneous endometrium, the concurrent presence of premenstrual bleeding alongside increased ET should immediately raise the index of clinical suspicion. Rather than relying on a rigid numerical scoring system or nomogram, the clinician should use these combined indicators as a threshold to ask, "Could there be an underlying focal lesion?", thereby justifying the decision to refer the patient to a tertiary center or to perform saline infusion sonography. This approach optimizes resource allocation and minimizes unnecessary invasive procedures in low-risk patients.

Strengths and Limitations

This study has several notable strengths. The prospective design allowed for systematic data collection, while performing all ultrasonographic examinations by a single experienced physician minimized interobserver variability. Furthermore, the large sample size provided robust statistical power to evaluate multivariable clinical predictors.

However, several limitations must be acknowledged. Most critically, the diagnosis of endometrial polyps was predominantly based on blind endometrial sampling rather than direct visualization via hysteroscopy or saline infusion sonography. Because polyps are inherently focal lesions, blind sampling carries a substantial risk of missing these pathologies, which inevitably introduces verification bias. Consequently, our model's performance reflects the likelihood of a biopsy-detectable pathology rather than the absolute true prevalence of polyps. Nevertheless, subjecting all patients with equivocal ultrasound findings to routine hysteroscopy without prior risk stratification would be neither ethically justified nor practically feasible in a resource-constrained setting.

Additionally, excluding patients with overtly suspected intrauterine lesions on initial ultrasonography likely introduced selection bias by underrepresenting larger polyps. However, this was a deliberate design choice aimed at evaluating subtle clinical predictors in the challenging diagnostic 'gray zone', rather than focusing on obvious cases that already have a clear management pathway. It should also be noted that the relatively high prevalence of polyps (42.2%) in our cohort is attributed to the tertiary referral

nature of our center and the specific inclusion of highly symptomatic patients who met the indications for biopsy. Finally, the exclusion of malignant cases ($n = 3$, 0.28%) was a methodological necessity to maintain statistical model integrity; given the exceptionally low incidence of endometrial carcinoma in reproductive-aged women, this exclusion does not compromise the real-world clinical applicability of our findings.

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