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Diagnostic Hysteroscopy in the Evaluation of Abnormal Uterine Bleeding During Perimenopause

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Abstract

Abnormal uterine bleeding is a common gynecological concern during perimenopause and may arise from structural endometrial or myometrial pathology, ovulatory dysfunction, or systemic and iatrogenic causes. The transition is associated with fluctuating ovarian function and irregular bleeding patterns, complicating clinical assessment. This narrative review discusses the classification and evaluation of abnormal uterine bleeding in perimenopausal women, with emphasis on the role of diagnostic hysteroscopy in assessing the uterine cavity. Clinical evaluation involves a detailed menstrual history, appropriate laboratory investigations, transvaginal ultrasonography, and endometrial sampling when indicated. Although ultrasonography is an accessible first-line imaging method, focal intracavitary lesions may require further assessment. Hysteroscopy permits direct visualization of the endometrium and targeted biopsy of suspicious abnormalities, including polyps and submucosal fibroids. In selected patients, operative hysteroscopy also enables a see-and-treat approach. Nevertheless, histopathological examination remains important when premalignant or malignant disease is suspected. Procedural selection should consider the location of pathology, clinical risk factors, patient tolerability, and safety. Hysteroscopy provides an important complementary approach to imaging and endometrial assessment in women with perimenopausal abnormal uterine bleeding.

Keywords: Perimenopause; Abnormal uterine bleeding; Hysteroscopy; Endometrial polyps; Uterine cavity; Endometrial biopsy

Introduction

Abnormal uterine bleeding (AUB) is a broad term that describes irregularities in the menstrual cycle involving the parameters of frequency, regularity, duration, and volume of flow outside of pregnancy in reproductive-aged women. Up to one-third of women will experience AUB in their life, with irregularities most commonly occurring at menarche and perimenopause. A normal menstrual cycle has a frequency of 24 to 38 days and lasts 2 to 7 days, with 5 to 80 mL of blood loss. Therefore, variations in any of these 4 parameters constitute AUB [(1)].

AUB terminology and classification have evolved to promote clarity and uniformity in diagnosis. Revisions to AUB terminology were first published in 2007, followed by updates from the International Federation of Obstetrics and Gynecology (FIGO) in 2011 and 2018. In 2007, FIGO System 1 established more defined descriptive terms nongestational AUB based on the frequency, regularity, duration, and volume of flow. The nonspecific terminology of menorrhagia, metrorrhagia, and oligomenorrhea was also replaced with the terms heavy menstrual bleeding (HMB) characterized by bleeding >80 mL or heavy enough to interfere with a patient's qualify of life, intermenstrual bleeding (ie, cyclical or random spontaneous bleeding between menstrual periods) and breakthrough bleeding on hormone medication [(2)].

FIGO System 2 introduced PALM-COEIN, which categorizes AUB into structural (polyp, adenomyosis, leiomyoma, malignancy/hyperplasia) and nonstructural (coagulopathy, ovulatory dysfunction, endometrial, iatrogenic, not otherwise classified) etiologies. The committee also defined irregular bleeding as any bleeding that falls outside the 5th to 95th percentiles for any menstrual parameter (eg, regularity, frequency, duration, and volume) [3].

Etiology and Classification of Abnormal Uterine Bleeding

The PALM-COEIN classification, established by FIGO, organizes the potential causes of AUB into the following structural and nonstructural categories, which aids in diagnosing and managing AUB effectively: [4]

Polyp (P): Endometrial or endocervical polyps are focal outgrowths of tissue that may be asymptomatic or cause intermenstrual bleeding. While most are benign, they occasionally carry a malignancy risk [5].

Adenomyosis (A): This condition involves the presence of endometrial tissue within the uterine muscle and is often associated with heavy, painful, or prolonged menstruation and may result in uterine enlargement [6].

Leiomyoma (L): Commonly known as fibroids, these benign smooth muscle tumors can lead to heavy or prolonged menstrual bleeding, particularly if large or submucosal. Many leiomyomas are asymptomatic [7].

Malignancy and hyperplasia (M): These include endometrial hyperplasia and cancers, often presenting with unpredictable bleeding. Risk factors include prolonged estrogen exposure without opposition by progesterone [8].

Ovulatory dysfunction (O): Conditions like polycystic ovary syndrome (PCOS), hypothalamic disorders, or thyroid dysfunction can lead to infrequent, irregular, heavy, or prolonged bleeding due to inconsistent ovulation [9].

Multiple factors may simultaneously contribute to a patient's AUB, and structural abnormalities (eg, polyps or leiomyomas) are not always the primary culprits. Diagnostic imaging techniques are vital in identifying structural causes, while nonstructural causes often require clinical and laboratory assessments for diagnosis. This array of etiologies underscores the complexity of AUB, emphasizing the need for individualized evaluation and treatment strategies [10].

Pathophysiology of Abnormal Uterine Bleeding

The pathophysiology of AUB reflects the intricate interplay between endocrine, immune, and vascular systems in the endometrium, where disruptions in these mechanisms can lead to irregularities in menstrual bleeding. Normal menstruation involves progesterone withdrawal at the end of the menstrual cycle, triggering a well-coordinated cascade of endometrial changes. These include epithelial and stromal apoptosis, inflammatory mediator release, and matrix metalloproteinase activation, which facilitate endometrial shedding and subsequent repair. Effective hemostasis requires spiral arteriole constriction, clot formation, and tissue regeneration. In individuals with AUB, these processes are dysregulated, leading to excessive or irregular bleeding [11].

AUB etiologies differ based on hormonal and structural influences, though the exact pathophysiologic mechanisms may be unclear. For instance, ovulatory dysfunction resulting in disruption of the hypothalamic-pituitary-ovarian axis arises from unpredictable progesterone withdrawal, leading to unregulated endometrial growth and shedding. In contrast, endometrial dysfunction is linked to impaired vascular and hemostatic responses, often involving diminished hypoxia signaling and abnormal endometrial repair [12].

Structural causes like fibroids and adenomyosis further complicate the picture, disrupting myometrial contractility, paracrine signaling, and vascular function. For example, fibroids may induce excessive bleeding through mechanisms, eg, increased endometrial surface area, altered angiogenesis, and impaired clotting factor expression. The precise mechanisms linking polyps to AUB have not been identified [13].

Clinical Evaluation and Imaging

The clinical assessment of abnormal uterine bleeding (AUB) involves a systematic evaluation aimed at identifying underlying causes and determining the severity of bleeding. Screening tools such as the Menstrual

Distress Questionnaire (MEDI-Q) can be useful in assessing the impact of heavy menstrual bleeding (HMB) on a patient's daily life, particularly in those with conditions like uterine fibroids. The first priority in evaluation is to assess hemodynamic stability. In patients presenting with acute AUB who are unstable, resuscitative measures must be initiated before proceeding with detailed history taking [(14)].

The diagnostic evaluation of abnormal uterine bleeding requires an integrated approach that combines laboratory testing, imaging studies, and endometrial assessment. This comprehensive strategy helps identify the underlying etiology, distinguish between structural and nonstructural causes, and guide appropriate and effective management [(15)].

In all reproductive-aged women, pregnancy must first be excluded using either a urine or serum human chorionic gonadotropin test. A complete blood count (CBC) should also be performed to assess for anemia and thrombocytopenia. Additional laboratory investigations are guided by clinical findings and should be performed when indicated [(16)].

Diagnostic imaging plays a key role in evaluating suspected structural causes of AUB. Imaging is generally indicated when abnormalities are detected on bimanual examination or when symptoms persist despite initial treatment. In adolescents, routine imaging is not typically recommended unless there is failure of initial management [(15)].

Transvaginal ultrasound (TVUS) and transabdominal ultrasound are the preferred first-line imaging modalities when imaging is indicated. These techniques are particularly effective in identifying structural abnormalities such as polyps, adenomyosis, and leiomyomas. In adolescent patients, transabdominal ultrasound is often preferred over transvaginal ultrasound [(17)].

Saline-infused sonohysterography may be used to improve detection of intracavitary lesions by introducing sterile saline into the uterine cavity during transvaginal ultrasound. However, its usefulness may be limited if the endometrium is not adequately visualized on initial ultrasound.

Endometrial sampling is recommended in patients aged 45 years or older who present with AUB, as advancing age is a significant risk factor for endometrial cancer. It is also indicated in younger patients with persistent bleeding, a history of prolonged unopposed estrogen exposure, or those who do not respond to medical management [(18)].

Office-based endometrial biopsy is considered the first-line method for sampling. If this approach is unsuccessful, yields insufficient tissue, or cannot be performed, hysteroscopic dilation and curettage is recommended. In cases where patients continue to have persistent symptoms despite normal biopsy results, hysteroscopy should be performed, as blind sampling techniques may fail to detect focal lesions [(19)].

Perimenopausal Abnormal Uterine Bleeding

Perimenopause is defined as the period of time during which a woman's body transitions towards menopause, or the final menstrual period. The beginning of the perimenopause phase is marked by the onset of menstrual irregularities, and menopause itself is retroactively confirmed after 12 months of amenorrhea.

Perimenopause brings about a host of changes within the body, mostly due to the decline in ovarian function, which results in decreased estrogen and progesterone production. The perimenopause phase is reported to last for an average of 4–7 years, though it can last up to 14 years, and the average age of menopause is 51–52 years in the US [(20)].

Bleeding patterns among women in the perimenopause vary, thus distinguishing between "normal" and "abnormal" can be difficult. In the early menopause transition, short cycle intervals (fewer than 21 days) are more common, while long cycle intervals (more than 36 days) occur later in the transition. During the menopausal transition, women were more likely to experience an increased number of days of bleeding, with 77% reporting at least 3 episodes of 10+ days of bleeding [(21)].

Abnormal uterine bleeding presents a unique challenge to the provider in the perimenopause, as physiologic hormonal changes may mimic, or mask pathologic diagnoses. These presentations often warrant further evaluation to rule out serious conditions such as hyperplasia or cancer, and to guide treatment options. For perimenopausal women, the PALM-COEIN classification of abnormal uterine bleeding applies and should be utilized to establish a differential diagnosis of bleeding and to guide evaluation and management [22].

Evaluation should include a thorough menstrual, medication, and family history, and assessment for endocrine dysfunction or bleeding disorders (when indicated). Examination should evaluate BMI, thyroid, uterus and cervix via both a speculum and bimanual assessment. This information will help guide laboratory testing, which may include complete blood count, iron studies, thyroid assessment, or evaluation for coagulation disorders.

Transvaginal ultrasonography is the imaging modality of choice to identify uterine and endometrial structural abnormalities, although further assessment with saline infusion sonohysterography (SIS) or office hysteroscopy may be warranted for evaluation of intracavitary lesions [23].

Endometrial biopsy is indicated for persistent abnormal uterine bleeding, or in the perimenopausal setting for those with risk factors, including chronic anovulation and obesity. While endometrial biopsy is sensitive in detecting global endometrial pathology, it is important to keep in mind that its sensitivity decreases for focal pathology. Once evaluation is complete, tailored management options can be discussed [24].

Perimenopausal AUB is any abnormal menstrual bleeding during menopausal transition or within the first year after menopause (except for cyclic bleeding in women using hormonal replacement therapy). AUB is the leading cause of approximately one-third of all outpatient gynecological visits, particularly in the perimenopausal period. More than 90% of women experience at least one episode of AUB, and 78% of them at least three episodes of AUB during their transition to menopause. The popular classification of nongestational causes of AUB was introduced by FIGO (International Federation of Gynecology and Obstetrics) in 2011 and revised in 2018 [22].

The causes of nongestational AUB have been classified into nine categories arranged according to the acronym PALM-COEIN, including the structural causes (“PALM”): polyp, adenomyosis, leiomyoma, malignancy/hyperplasia, and non-structural causes (“COEIN”): coagulopathy, ovulatory dysfunction, endometrial, iatrogenic, and “not otherwise classified”. The contribution of individual PALM-COEIN categories to the spectrum of AUB causes changes with age; nevertheless, endometrial polyps and fibroids remain the most common structural causes of AUB in perimenopause. In the fourth decade of life, the impact of myomas and adenomyosis as AUB causes increases. Likewise, the highest incidence of endometrial polyps is reported in women aged 40–44 years. Notably, the rate of structural pathologies (fibroids, polyps, adenomyosis) coexisting with each other or with uterine malignancies also increases with age [25].

Additionally, various local or systemic conditions, and hormonal or non-hormonal medications (tamoxifen, oral anticoagulants), can trigger uterine bleeding. Hematologic dysfunctions are also a frequent cause of AUB in perimenopausal women, being reported as the cardinal symptom in 32–100% of women with von Willebrand factor deficiency (relevant to 0.5–1% of the general population), in 5–98% of women with platelet dysfunction, and 35–70% of women with rare factor deficiencies. Although the annual probability of spontaneous conception is about 10% by age 40–44, falling to 3% by age 45–49, the percentage of women fulfilling their reproductive goals in their fourth decade is continuously rising. However, 84% of pregnancies in women over 48 years end in first-trimester miscarriage, and the rate of ectopics in women over 44 years rises to 7%. Therefore, up to 12 months after FMP, excluding pregnancy is a mandatory part of the AUB diagnostic workup [14].

Role of Hysteroscopy in Uterine Cavity Assessment

The gold standard for the diagnosis and treatment of intrauterine pathology is hysteroscopy. As such, this technique has numerous indications and benefits. Hysteroscopy can improve quality of life, treat infertility, remove foreign bodies, or diagnose malignancy. Women with abnormal uterine bleeding may experience

significant improvement in symptoms post hysteroscopic resection of pathology, avoiding the need for invasive surgical procedures such as hysterectomy [26].

Also, compared to blind endometrial sampling, direct visualization of the entire uterine cavity and biopsy with hysteroscopy allows for targeted sampling and complete resection of uterine abnormalities such as polyps. These have the potential for malignancy, especially in postmenopausal women and women with a family history of gynecologic cancer. Further, ambulatory hysteroscopy offers appeal with the potential avoidance of general anesthesia or conscious sedation. Studies comparing in-office to operating room hysteroscopy show comparable patient acceptance and outcomes, as well as decreased cost [27].

Hysteroscopy involves inserting a rigid or flexible hysteroscope through the cervical canal into the uterus and then using distending media to allow for complete visualization of the endometrial cavity. The type of distending media is selected based on the type of energy that will be used.

With the invention of smaller hysteroscopes with reduced diameters and more technically advanced operating systems, in-office hysteroscopy has become a widely accepted method for diagnosing and treating intrauterine pathology.

A new concept gaining popularity is the "see-and-treat" strategy, in which the patient is diagnosed during office hysteroscopy with an intrauterine organic pathology, eg, endometrial polyps or thickened endometrium. This identified pathology can then be treated hysteroscopically during the same visit. The see-and-treat strategy has all the same indications, and more, compared to traditional hysteroscopy, including thickened endometrium, endometrial pathology, retained products of conception, and retained foreign bodies. Polypectomy is the most common hysteroscopic procedure worldwide and can be easily transitioned to be performed through the see-and-treat method [28].

Hysteroscopy is considered the gold standard technique for diagnosing and managing pathological conditions affecting the uterine cavity. In turn, AUB is the most common indication to perform hysteroscopy in perimenopausal women. The hysteroscopic "see-and-treat" approach allows exploration of the uterine cavity, targeted endometrial and endocervical biopsies, and—if indicated—immediate treatment of endocervical, endometrial, or submucosal pathologies (polyps, myomas) [29].

It is essential to highlight that hysteroscopy is unsuitable for evaluating and treating deep myometrial pathologies (such as adenomyosis or myomas FIGO-Grade $\geq$ 3). Most hysteroscopic procedures can be performed in an office setting depending on the patient's preferences, available infrastructure (staffing, equipment), surgeon's experience, and comfort level. More complex and prolonged procedures, such as hysteroscopic myomectomy and extensive lysis of intrauterine adhesions, are typically performed in the operating room, thus providing the patient with general anesthesia and the ability of the surgeon to perform more extensive surgery. Moreover, hysteroscopy can be complemented with laparoscopy if necessary. Regardless of the setting in which the hysteroscopic procedure is completed, it is helpful to distinguish diagnostic and operative hysteroscopy [30].

Diagnostic Hysteroscopy and Endometrial Pathology

Diagnostic hysteroscopy aims to diagnose lesions within the endometrial cavity and, if necessary, to obtain targeted biopsies. Diagnostic hysteroscopy can be a single intervention or may immediately precede hysteroscopic surgery. The feasibility of diagnostic hysteroscopy decreases in patients with previous surgeries, pelvic infections, IUD use, and postmenopausal status. A predictive score was developed for office hysteroscopy failure using different predictors, the most significant of which were history of procedures on the cervix, cesarean section, recurrent vaginitis, retroflexed uterus, and menopause. Depending on the previously indicated factors, office hysteroscopy could not be completed in 6 to 76% of the interventions [31].

Similarly, the terms "hysteroscopy" and "hysteroscopic view" were used interchangeably, reporting a low sensitivity (0.64 and 0.61) and specificity (0.92 and 0.95) for the diagnosis of endometrial hyperplasia. In another study, the concordance between the final histopathological result and the hysteroscopic impression was 86% for benign disease or normal endometrium, but only 58% for endometrial hyperplasia. In addition, the

lowest agreement (52%) was noted for postmenopausal endometrial hyperplasia. When restricted to women with postmenopausal AUB, the sensitivity and specificity of in-office hysteroscopy for endometrial hyperplasia (with histopathology as reference) was 87% and 43%, respectively. In contrast, it was not only confirmed that the diagnostic superiority of hysteroscopy with an eye-directed biopsy for detecting endometrial pathologies compared to TVS (and thus recommended hysteroscopy for all postmenopausal women with AUB and endometrial thickness > 4 mm) but also demonstrated the unique efficiency of hysteroscopy for diagnosing focal abnormalities (including EC) in the atrophic endometrium that would otherwise likely be missed by TVS. The authors advocate hysteroscopic evaluation even in patients with AUB with endometrium on TVS of <4 mm, aiming to decrease the chance of failing to diagnose carcinomas that develop focally in the atrophic endometrium [(32)].

Less threatening but a more common finding in patients with AUB (20–31% of cases) are endometrial polyps. The sensitivity of TVS for the diagnosis of polyps is particularly low (0.51). In contrast, in women with postmenopausal AUB, the sensitivity and specificity of hysteroscopy for the diagnosis of polyps are reported at 0.81–0.92 and 0.85–0.98, respectively. Another study confirmed the superiority of diagnostic hysteroscopy (96.4% sensitivity, 74.6% specificity) in comparison to TVS (88.7% sensitivity, 25.4% specificity) for detecting endometrial polyps in women aged 41 to 82 presenting with AUB. Saline Infusion Sonohysterogram (SIS) provides a similar sensitivity compared with hysteroscopy but lower specificity (0.93 and 0.83 compared to 0.95 and 0.90, respectively).

Similarly, hysteroscopy offers the highest diagnostic accuracy (>90%) for detecting submucous myomas as compared to TVS or SIS. Further developments in the field of sonography, based on the three-dimensional virtual image synthesis (so called “virtual sonographic hysteroscopy”), will show to what extent diagnostic hysteroscopy could be replaced by next-generation, three-dimensional imaging modalities for detecting intracavitary uterine pathologies [(33)].

Quality of Life

When considering the mutual relation between hysteroscopy, AUB, QoL, and sexuality, it is necessary to address the interplay of the following factors: bleeding (with/without anemia), underlying conditions (e.g., menopausal status, cancer), treatments (effectiveness, discomfort caused during the procedure), over- or undertreatment (need to perform surgical procedures), age and menopausal status (regardless of AUB or its treatments), and the controversy about the impact of hysterectomy (regarding uterus-preserving techniques) on QoL and sexuality [(34)].

Perimenopausal symptoms critically impairing QoL include sleep disturbances, fatigue, and anxiety. AUB can further compromise the overall health status and the health-related QoL (HRQOL), its sequelae (e.g., iron deficiency anemia, chronic fatigue), or associated comorbidities (e.g., pelvic pain). The treatment of endometriosis, myomas, and polyps leads to the best HRQoL scores, while treating nonspecific pelvic pain and AUB is less frequently associated with HRQoL improvement. Post-AUB anemia has a detrimental impact on a woman’s QoL by interfering with physical activity, vitality, cognition, work performance, and social and emotional life. In addition, age alone is one of the strongest independent factors compromising the QoL in women with AUB [(35)].

Operative Hysteroscopy and Procedural Safety

Operative hysteroscopy uses mechanical, electrosurgical, and laser instruments to treat intracavitary pathologies. The introduction of the small-diameter coaxial bipolar electrode (Versapoint, Gynecare, Ethicon, NJ, USA) in 1999 was a milestone for outpatient operative hysteroscopy. The development of miniaturized mechanical instruments with small diameter scopes and working channels with continuous flow systems enabled the “see-and-treat” approach without general anesthesia. It was confirmed that major operative hysteroscopic surgery could be performed in an office-based setting resulting in a 98.8% rate of “satisfied” or “very satisfied” patients. Both outpatient (73%) and inpatient (80%) hysteroscopic polypectomy offer comparable success rates, as determined by the patients’ subjective bleeding and QoL assessment after six months. However, procedure

failure is higher (19% vs. 7%), and acceptability is lower (83% vs. 92%) with outpatient compared to inpatient polypectomy.

Conclusion:

Diagnostic hysteroscopy allows direct uterine cavity assessment and targeted endometrial sampling in women with perimenopausal abnormal uterine bleeding. It complements clinical evaluation and ultrasonography, particularly when focal intracavitary pathology is suspected. Histopathological confirmation remains necessary when endometrial hyperplasia or malignancy is a concern, and the benefits of hysteroscopic intervention should be balanced against procedural risks and patient preferences.

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