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Management of Endometrial Intraepithelial Neoplasia or Atypical Endometrial Hyperplasia

Committee on Clinical Consensus–Gynecology. This Clinical Consensus was developed by the American College of Obstetricians and Gynecologists' Committee on Clinical Consensus–Gynecology in collaboration with Lori Boardman, MD, Akiva P. Novetsky, MD MS, and Fidel Valea, MD.
The Society of Gynecologic Oncology endorses this document.

Summary

Endometrial intraepithelial neoplasia (EIN) or atypical endometrial hyperplasia (AEH) often is a precursor lesion to adenocarcinoma of the endometrium. Hysterectomy is the definitive treatment for EIN–AEH. When a conservative (fertility-sparing) approach to the management of EIN–AEH is under consideration, it is important to attempt to exclude the presence of endometrial cancer to avoid potential undertreatment of an unknown malignancy in those who have been already diagnosed with EIN–AEH. Given the high risk of progression to cancer, those who do not have surgery require progestin therapy (oral, intrauterine, or combined) and close surveillance. Although data are conflicting and limited, studies have demonstrated that treatment with the levonorgestrel-releasing intrauterine device results in a higher regression rate when compared with treatment with oral progestins alone. Limited data suggest that cyclic progestational agents have lower regression rates when compared with continuous oral therapy. After initial conservative treatment for EIN–AEH, early detection of disease persistence, progression, or recurrence requires careful follow-up. Gynecologists and other clinicians should counsel patients that lifestyle modification resulting in weight loss and glycemic control can improve overall health and may decrease the risk of EIN–AEH and endometrial cancer.

BACKGROUND

Endometrial intraepithelial neoplasia (EIN) or atypical endometrial hyperplasia (AEH), depending on classification system used, is of clinical significance because often it is a precursor lesion to adenocarcinoma of the endometrium (1, 2). There currently are two systems of endometrial precancer nomenclature in common usage. The WHO94 schema, which proposed four categories of risk classification based on glandular complexity and nuclear atypia, was updated in 2014 to a two-tiered system: 1) hyperplasia without atypia (benign endometrial hyperplasia) and 2) atypical hyperplasia or EIN (3–5). Subsequently, the 2020 World Health Organization classification expanded on the diagnostic criteria in the two-tiered system to include essential and desirable criteria (6). Essential criteria

SUMMARY OF CONSENSUS RECOMMENDATIONS

Detecting Concurrent Carcinoma

Gynecologists should attempt to exclude concurrent carcinoma in individuals with a working diagnosis of EIN–AEH. Hysteroscopic examination with further sampling of the endometrium is the most accurate method for detecting a concurrent carcinoma.

Surgical Management

Hysterectomy is the definitive treatment for EIN–AEH. Gynecologists should not perform supracervical hysterectomy for the treatment of EIN–AEH.

Gynecologists should not perform endometrial ablation (thermal or electrocautery) for EIN–AEH due to high persistence and recurrence rates, as well as potential difficulty in evaluating future bleeding episodes.

Nonsurgical Management

Clinicians should recommend progestational agents as treatment for EIN–AEH for patients in whom hysterectomy is not an option.

Data on the superiority of either oral or intrauterine progestational agents are lacking, though limited data suggest that intrauterine progestational administration may be associated with a higher rate of disease regression when compared with oral administration alone in patients with EIN–AEH.

There is insufficient evidence to recommend any one formulation of oral progestational agent over another.

Follow-up

For those initially treated with progestational agents, gynecologists should perform repeat histologic assessment for response to treatment for EIN–AEH within 3–6 months.

After initial progestin treatment, gynecologists may consider long-term maintenance therapy with progestational agents for patients with continuing risk factors for endometrial cancer.

Counseling Patients on Lifestyle Modifications

Gynecologists and other clinicians should counsel patients that lifestyle modification resulting in weight loss and glycemic control can improve overall health and may decrease the risk of EIN–AEH and endometrial cancer.

EIN–AEH, endometrial intraepithelial neoplasia or atypical endometrial hyperplasia.

for atypical hyperplasia or EIN include crowded glandular architecture and altered epithelial cytology distinct from the surrounding endometrium or entrapped nonneoplastic glands or both. Desirable criteria include the following: loss of immunoreactivity for PTEN, PAX2, or mismatch repair proteins. In the EIN schema developed by the International Endometrial Collaborative Group, endometrial precancer is termed endometrial intraepithelial neoplasia, and pathologic criteria were used to develop three disease categories: 1) endometrial hyperplasia, 2) endometrial intraepithelial neoplasia, and 3) adenocarcinoma (7). The American College of Obstetricians and Gynecologists (ACOG) does not recommend one terminology schema over another. This topic has been updated to reflect newer data on the management of EIN–AEH. This guidance applies to those patients who have already received a diagnosis of EIN–AEH.

Epidemiology

Estrogenic stimulation of the endometrium, unopposed by progestins, causes proliferative glandular epithelial changes or hyperplasia. Hyperplasia, due to prolonged exposure to estrogens, is biologically distinct from the precancerous lesion EIN–AEH. The precursor lesion of type I endometrioid adenocarcinoma is EIN–AEH. Making the distinction between hyperplasia and EIN–AEH is important, because each condition has differing cancer risks and requires different interventions to avoid undertreatment or overtreatment.

Cancer of the endometrium is rising in the United States, with an estimated incidence of 66,200 cases and 13,030 deaths in 2023 (8). Disparities in care linked to differences in race, ethnicity, geography, and socioeconomic status have been associated with poorer

outcomes. Data show that Black individuals with endometrial cancer have a 55% higher 5-year mortality risk when compared with White individuals (9). Although Black patients are more likely to be diagnosed with nonendometrioid (aggressive) histologies (10), this alone does not explain the disparity in mortality. Survival by Black individuals is lower than for White individuals, even when controlling for stage, grade, histologic subtype, and age. Asian/Pacific Islander patients also have been found to more frequently present with advanced disease when compared with White patients (11), and Black, Hispanic, and American Indian/Alaska Native individuals are less likely to receive guideline-compliant treatment (10). In addition to disparities by race and ethnicity, factors such as insurance status (Medicaid or Medicare vs private payer) and treatment at low-volume medical centers are associated with decreased survival rates (11). In a separate study, having Black and Hispanic race and ethnicity, Medicaid insurance or no insurance, and lower rates of education was associated with longer wait times for surgery after diagnosis (12).

METHODS

This Clinical Consensus document was developed using an a priori protocol in conjunction with the authors listed above. The a priori protocol was modeled after the Clinical Consensus methodology, and a full description of the Clinical Consensus methodology is published separately (13). The description below is specific to this Clinical Consensus document.

Literature Search

A literature search was performed from 2000 to October 2021 combining terms for endometrial hyperplasia and endometrial intraepithelial neoplasia with terms related to concepts in the outline. The ACOG medical librarians searched Cochrane Library, EMBASE, PubMed, and MEDLINE for human-only studies written in English. Cochrane trials from the Cochrane Collaboration Registry of Controlled Trials from 2016 to October 2021 were also saved. MeSH terms and keywords can be found in Appendix 1 (available online at http://links.lww.com/AOG/D269). Search terms for racial, ethnic, socio-economic, and vulnerable population disparities in EIN–AEH were incorporated into the literature review, and recommendations were drafted with the intent of promoting health equity and reducing these disparities. A bridge literature search was completed in March 2023. Any updated literature was incorporated into the text and recommendations, as appropriate.

Study Selection

Qualifying studies passed both title and abstract screen and full-text screen and met the following inclusion criteria: conducted in countries ranked very high on the United Nations Human Development Index (14), included female participants, and included all study designs. Studies that passed full-text screen by the authors were included in a summary evidence map (Appendix 2, available online at http://links.lww.com/AOG/D270). In one case, a study was identified after the literature search was concluded that did not meet one of the inclusion criterion (15). Although the study was conducted in a country that is not ranked as very high on the United Nations Human Development Index, the data were deemed necessary to demonstrate the comparative regression efficacy of combined intrauterine and oral progestins compared with the levonorgestrel-releasing intrauterine device (LNG-IUD) alone.

Consensus Voting and Recommendation Development

At a meeting of the Committee on Clinical Consensus–Gynecology, a quorum of two-thirds of eligible voting members was met, and the committee held a formal vote for each proposed recommendation. All recommendation statements met or exceeded the 75% approval threshold required for consensus.

Use of Language

The American College of Obstetricians and Gynecologists recognizes and supports the gender diversity of all patients who seek obstetric and gynecologic care. In original portions of this document, authors seek to use gender-inclusive language or gender-neutral language. When describing research findings, this document uses gender terminology reported by investigators. To review ACOG's policy on inclusive language, see https://www.acog.org/clinical-information/policy-and-position-statements/statements-of-policy/2022/inclusive-language.

Box 1. Progestational Agents for Treatment of Endometrial Intraepithelial Neoplasia or Atypical Endometrial Hyperplasia

- Megestrol acetate
- Medroxyprogesterone acetate
- Levonorgestrel-releasing intrauterine device
- Levonorgestrel-releasing intrauterine device plus oral progestin

DETECTING CONCURRENT CARCINOMA

Gynecologists should attempt to exclude concurrent carcinoma in individuals with a working diagnosis of EIN–AEH. Hysteroscopic examination with further sampling of the endometrium is the most accurate method for detecting a concurrent carcinoma.

The percentage of patients diagnosed with EIN–AEH who undergo hysterectomy and have endometrial cancer in the hysterectomy specimen ranges from approximately 30% to nearly 50% (16–18). Thus, when a conservative (fertility-sparing) approach to the management of EIN–AEH is under consideration, it is important to attempt to exclude the presence of endometrial cancer to avoid potential undertreatment of an unknown malignancy in patients who have been already diagnosed with EIN–AEH. Multiple methods are available to sample the endometrium. The simplest method, in-office suction endometrial sampling performed with a plastic cannula, has a long history of safety and efficacy and previously was found to be comparable with uterine curettage when used to diagnose endometrial cancer in women with abnormal bleeding (19). However, more recent data demonstrate a higher rate of endometrial cancer in hysterectomy specimens in patients with preoperative office Pipelle biopsy when compared with uterine dilation and curettage (20,21). It is believed that "mass lesions" that impinge on the endometrial cavity may deflect the pliable suction catheter and lead to ineffective sampling that may miss endometrial pathology.

Hysteroscopic-guided uterine sampling is recommended, and data demonstrate its utility for the diagnosis of endometrial polyps, endometrial cancer, and endometrial hyperplasia (22,23). There are several tissue-removal devices on the market that can provide simple, hysteroscopic-guided resection of the endometrium. Although they morcellate the specimen, this is done in a contained environment and produces excellent samples to evaluate, at the expense of clear orientation. Sampling methods that yield crushed or very small samples (jawed devices) or cauterized samples (hot loops) are not recommended, because it is difficult to adequately evaluate the pathologic specimen due to the artifact produced by the sampling method.

SURGICAL MANAGEMENT

Hysterectomy is the definitive treatment for EIN–AEH. Gynecologists should not perform supracervical hysterectomy for the treatment of EIN–AEH.

The primary objectives in the management of a patient with EIN–AEH are to 1) rule out endometrial cancer and 2) design a treatment plan that can prevent or delay progression to endometrial cancer. In a 2020 systematic review and meta-analysis, the risk of EIN–AEH progressing to endometrial cancer was approximately 8% per year (18). Patients may choose to undergo hysterectomy as definitive treatment for EIN–AEH. Depending on the clinical situation, some patients, such as those who desire to preserve fertility, may choose less definitive but still effective treatment strategies. Advantages of management with hysterectomy include definitive assessment of a possible concurrent carcinoma (occurring in approximately 30–50% of cases of EIN–AEH) and effective treatment of premalignant lesions that require no further therapy or specific follow-up for EIN–AEH (17,21,24). The decision to perform an oophorectomy in premenopausal individuals should be a shared decision between the patient and clinician due to the risks associated with surgical menopause (eg, cognitive impairment and cardiovascular disease) (25). These potential risks should be weighed against the risk of concurrent occult endometrial cancer; in this case, oophorectomy may be advised. Importantly, supracervical hysterectomy for the treatment of EIN–AEH should not be performed because of the inability to assess the lowest extent of the lesion; it may involve the lower uterine segment or upper endocervix.

Due to the high rate of concurrent endometrial cancer in patients with EIN–AEH, when performing a hysterectomy, the surgeon should consider intraoperative assessment of the uterine specimen for occult carcinoma because it may identify the need for additional surgical management. This intraoperative evaluation should be directed by a qualified pathologist or a surgeon with experience in evaluating uteri with endometrial cancer and should include gross examination of the open specimen and possible frozen section (26). The decision to consult a gynecologic oncologist should be individualized based on the patient and the health system's available resources (27). In settings without access to local oncology expertise, there is no role for intraoperative assessment of the specimen. If morcellation of the uterine specimen is needed to remove the uterus, it should be done in a contained environment (eg, a bag) to prevent any spill. Additionally, the surgeon should be aware that morcellation may make it more difficult for the pathologist to evaluate the specimen.

Gynecologists should not perform endometrial ablation (thermal or electrocautery) for EIN–AEH due to high persistence and recurrence rates, as well as potential difficulty in evaluating future bleeding episodes.

Endometrial ablation (thermal or electrocautery) should not be used to treat EIN–AEH. The U.S. Food and Drug Administration includes the following contraindication for the thermal (radio-frequency) endometrial ablation device: "A patient with known or suspected

endometrial carcinoma (uterine cancer) or pre-malignant change of the endometrium, such as unresolved adenomatous hyperplasia" (28).

NONSURGICAL MANAGEMENT

Clinicians should recommend progestational agents as treatment for EIN–AEH for patients in whom hysterectomy is not an option.

For some patients, hysterectomy may not be the most optimal strategy for treatment of EIN–AEH. Given the high risk of progression to cancer, patients who do not have surgery require progestin therapy and close surveillance. Many of the data on the use of progestational agents are derived from the treatment of patients with simple and complex hyperplasia, often in the absence of cellular atypia. In those populations, treatment with progestational agents has been shown to result in high rates of regression (29–37). Although there are more limited data on the treatment of EIN–AEH with progestational agents, studies have found high rates of disease regression in patients who are not candidates for definitive surgical management and, instead, are managed with more conservative approaches. A systematic review of outcomes in patients with EIN–AEH or grade 1 adenocarcinoma demonstrated an initial response to progestins of 86%, with a complete response (resolution) of 66% for those with EIN–AEH (38). Oral, intrauterine, and combined modes of administration have been shown to be effective, with rates of disease regression ranging from nearly 50% to greater than 90%, depending on study and method of administration (15,38–44). Data support that continuous oral therapy is more effective than the use of cyclical therapy (40). Among all methods, adverse effects were generally well-tolerated by patients. Vaginal bleeding may be more common with the intrauterine mode of administration, and nausea may be more associated with oral progestational agents. Data on use of the LNG-IUD for management of EIN–AEH are from the 52-mg LNG-IUD, with a delivery rate of 20 micrograms/day (15,41,42,44–48). Throughout this article, discussion of the LNG-IUD will refer to the 52-mg device with a delivery rate of 20 micrograms/day within 5 years of placement. See Box 1 for progestational agents used for the treatment of EIN–AEH.

Data on the superiority of either oral or intrauterine progestational agents are lacking, though limited data suggest that intrauterine progestational administration may be associated with a higher rate of disease regression when compared with oral administration alone in patients with EIN–AEH.

Although data are conflicting and limited, studies have demonstrated that treatment with the LNG-IUD results in a higher regression rate when compared with treatment with oral progestins alone (15, 40, 47). Continuous oral progestins do demonstrate efficacy in the treatment of EIN–AEH; one randomized trial found it to be nearly as effective as treatment with the LNG-IUD (40). One study observed an improved regression rate with combined intrauterine and oral progestins (85%) compared with the LNG-IUD alone (55%) (15).

Compared with systemic therapy, adverse events with the LNG-IUD are uncommon and similar to those reported when the LNG-IUD is used for contraception (eg, expulsion, perforation, pelvic inflammatory disease). Additionally, patient adherence with LNG-IUD therapy has been reported to be higher, with less weight gain, and patient-reported health status scores (physical functioning and energy levels) have been reported to improve over time with this method (44,49). The American College of Obstetricians and Gynecologists supports insurance coverage for the most appropriate progestin therapy method for the patient based on individualized risks, benefits, and preferences.

There is insufficient evidence to recommend any one formulation of oral progestational agent over another.

To date, no direct comparisons between different oral progestin formulations have been published. However, megestrol acetate or medroxyprogesterone acetate are recommended given that the majority of studies on management of EIN–AEH with progestational agents used one of these two agents. Limited data suggest that cyclic progestational agents have lower regression rates when compared with continuous oral therapy (40).

FOLLOW-UP

For patients initially treated with progestational agents, gynecologists should perform repeat histologic assessment for response to treatment for EIN–AEH within 3–6 months.

After initial conservative treatment for EIN–AEH (treatment with progestational agents), early detection of disease persistence, progression, or recurrence requires careful follow-up. The initiation and frequency of histologic assessment depends on numerous factors, including the choice of treatment, menopausal status, and the presence of obesity and other risk factors associated with endometrial cancer. Surveillance after total hysterectomy for EIN–AEH with pathologic confirmation of the absence of coexisting endometrial carcinoma is not recommended, because surgery eliminates the risk of disease progression (24).

For patients managed with progestational agents, repeat histologic assessment within 3–6 months is recommended to determine treatment response. There are several types of potential outcomes to treatment (50). The first is resolution (complete response) of the

hyperplasia, with a repeat endometrial sampling demonstrating atrophic, secretory, or proliferative endometrium. Secondly, regression is considered to have occurred when the repeat sampling still reveals hyperplasia but without atypia. The third type of outcome is persistence of disease with no change in histology at the time of the repeat sampling. Finally, there can be progression to cancer. Review of the biopsy results and consultation with a pathologist may assist with the individualization of a patient's follow-up plan. If there is no response or some regression during the initial 3–6 months of therapy, an additional 3–6 months of therapy may be considered after discussion with the patient. If there is no response after 9–12 total months of therapy, other management options, including definitive surgery, should be discussed.

In a systematic review of 111 women with EIN–AEH and 280 women with early-stage endometrial carcinoma treated with progestational agents, the median time to complete response (resolution), in studies in which time to response was reported, was 6 months (ranging from 1 to 18 months) (38). After 3 months of treatment, failure to detect exogenous progesterone effect is associated with lack of response (44). Nonresponse after 6 months of treatment with the LNG-IUD was associated with increased uterine diameter (9.3 vs 8 cm; *P*=.04) (51). Whether it is preferable to discontinue oral progestins and wait for a withdrawal bleed before endometrial sampling or proceed with sampling while the patient continues oral progestin treatment remains unclear (24). In patients being treated with the LNG-IUD, histologic sampling may be completed with the device in place. The utility of pretreatment hormone receptor expression (PR-A and PR-B) in predicting relapse after progestin-based therapy has been demonstrated (52–54).

The optimal interval and duration of endometrial sampling after complete response (resolution) with treatment with progestational agents have not been established (38,55). In a retrospective observational cohort study of 245 women with EIN–AEH managed with suction dilation and curettage to rule out occult malignancy followed by treatment with LNG-IUD or oral progestin therapy, 28 patients (11.4%) progressed to cancer, with a median time to cancer diagnosis of 9.5 months (interquartile range 3.5–28.6 months) (46). Based on what is known about potential progressive disease, it is reasonable to continue endometrial sampling in patients treated with progestational agents every 3–6 months for up to 2 years. The recurrence rate of EIN–AEH remains elevated after initial response to conservative management with progestational agents.

A systematic review reported a recurrence rate of approximately 23% for patients treated for EIN–AEH (n=111) and a median time to recurrence of 24 months (ranging 4–72 months) for those treated for EIN–AEH or grade 1 adenocarcinoma (n=391) (38). Some experts recommend discontinuing surveillance biopsies after 2 years for patients without evidence of persistent disease, recurrence, or progression of disease and who are asymptomatic without vaginal bleeding. However, both patients and clinicians should be vigilant of clinical changes, such as symptoms of recurrence (eg, vaginal bleeding), and the need for follow-up (biopsy, pathology review, or consultation with a gynecologic oncologist).

After initial progestin treatment, gynecologists may consider long-term maintenance therapy with progestational agents for patients with continuing risk factors for endometrial cancer.

After initial treatment with progestational agents, medical management with these agents may be continued in patients who remain at risk for the development of endometrial cancer due to the following: factors such as increasing age, late menopause, nulliparity, and chronic anovulation; higher-risk conditions (Lynch syndrome, Cowden syndrome); modifiable risk factors, such as the use of unopposed estrogen therapy; and potentially modifiable risk factors, such as obesity and type 2 diabetes mellitus. In a case–control study of 138 women diagnosed with endometrial cancer at least 1 year after an index biopsy of endometrial hyperplasia and a matched control group, the risk of progression of the 42 women with atypical hyperplasia (all of whom received hormonal treatment [eg, medroxyprogesterone acetate]) to carcinoma was 8.2% through 4 years (95% CI 1.3–14.6%); cumulative risk steadily rose to 27.5% (95% CI 8.6–42.5%) at 19 years after the index biopsy (56). Most studies, however, have follow-up periods of insufficient length to inform approaches to long-term maintenance. Guidance on how long to continue the use of an LNG-IUD or systemic progestational agents to prevent long-term recurrence has not been determined.

Future Fertility

A systematic review and systematic review and meta-analysis focused on fertility-sparing therapy for premenopausal women with EIN–AEH reported pregnancy rates ranging from 26.3% to 41.0% for premenopausal individuals who opted for management with progestational agents (38, 43). For those who received fertility-sparing treatment for EIN–AEH or endometrial cancer, the use of assisted reproductive technology was common (57), and the live-birth rate in women using assisted reproductive technology was higher than that of women who attempted to achieve pregnancy spontaneously (39.4% vs 14.9%; *P*=.001) (43). A retrospective analysis of 63 patients (42 with endometrial cancer and 21 with EIN–AEH) who underwent fertility-sparing treatment reported that, of the 31 patients who achieved remission with medroxyprogesterone acetate and metformin, in vitro fertilization and embryo transfer resulted in 19 pregnancies

(61.3%) and 14 live births (45.2%) (58). A small prospective cohort study (n=60) found that in vitro fertilization after conservative fertility-sparing management of EIN–AEH or grade 1 endometrial adenocarcinoma was not associated with an increased risk of recurrence (59). Because many patients will have conditions that can negatively affect fertility (eg, polycystic ovarian syndrome, obesity, and diabetes), active management to achieve pregnancy should be discussed and referral to an infertility specialist should be considered.

COUNSELING PATIENTS ON LIFESTYLE MODIFICATIONS

Gynecologists and other clinicians should counsel patients that lifestyle modification resulting in weight loss and glycemic control can improve overall health and may decrease the risk of EIN–AEH and endometrial cancer.

More than 75% of endometrial cancer survivors have obesity (60), defined as having a body mass index (BMI [calculated as weight in kilograms divided by height in meters squared]) of 30 or higher. They are more likely to have obesity-related comorbidities and are at a greater risk of mortality compared with those without obesity. Many individuals who receive gynecologic care, including those in treatment for EIN–AEH or carcinoma as well as survivors, are unaware of the link among obesity, endometrial hyperplasia and cancer, and other comorbidities, including hypertension and type 2 diabetes (60–64). Weight loss of 7–10% of a person's total body weight has been found to have positive effects on health outcomes. Education, counseling on options for lifestyle modification leading to weight loss and improved glycemic control, and shared decision making are components of care that have the potential to affect immediate and long-term outcomes.

Gynecologists may consider counseling patients being treated with an LNG-IUD for EIN–AEH who also have obesity about weight-loss interventions. In a prospective study of 71 women with atypical hyperplasia or grade 1 or 2 endometrioid adenocarcinoma being treated with the LNG-IUD, investigators assessed the uptake of bariatric surgery (offered to those with BMIs higher than 35) and the effects of more than 10% of body weight loss on progestin treatment response at 12 months (48). Ninety percent of participants were offered bariatric surgery, and 36% subsequently underwent a bariatric procedure. The remaining patients were encouraged to follow a low-calorie diet. Of 71 participants, 43 (61%) responded to treatment, 23 (32%) had stable disease, and five (7%) progressed during treatment with an LNG-IUD. Excluding those who progressed, women who lost more than 10% of their total body weight (86% of bariatric patients and 23% of patients on low-calorie diets) were nearly four times more likely to respond to the LNG-IUD (adjusted odds ratio 3.95, 95% CI 1.3–12.5; *P*=.02) (48). Telemedicine and text-based weight-loss interventions for individuals with endometrial hyperplasia or type 1 endometrial cancer and obesity have demonstrated effectiveness in assisting patients with weight loss (62). Discussions about the diagnosis of EIN–AEH or early-stage endometrial cancer may be a useful time to discuss potential lifestyle modifications and related tools for weight loss.

FURTHER RESEARCH

Limitations of the current literature include the use of inconsistent terminology for endometrial hyperplasia and, in many trials, the inclusion of individuals with endometrial hyperplasia without atypia. Although focus on EIN–AEH is increasing, further research and larger sample sizes are needed. Research should include patient-centered outcomes, with an emphasis on patient quality of life. To better understand optimal approaches to the management of EIN–AEH and existing disparities in treatment and mortality, more research is needed on the causes of disease relapse and regression, particularly in historically excluded populations, including Black, Hispanic, and Indigenous patients. More research is needed to identify treatments and interventional approaches that can eliminate disparities and ensure equity for all patients.

The number of individuals with risk factors for EIN–AEH—in particular obesity—is increasing. More data are needed on potentially modifiable risk factors, including rigorous and adequately powered randomized controlled trials with adequate duration of follow-up focusing on the effects of dietary modifications, as well as medical and surgical weight-loss management.

Additionally, research is needed on the utility of repeat sampling for the exclusion of concurrent malignancy when diagnosing EIN–AEH, the comparative effectiveness of different progestational agents, and the subtypes of EIN–AEH, including molecular classification. Long-term outcomes of patients who did not have definitive treatment (hysterectomy) are needed. The effect of combination therapies for initial nonresponders, the utility of lower-dose LNG-IUDs, and alternative approaches to monitoring patients with EIN–AEH are other areas of needed research.

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Appendices

1. Literature Search Strategy: http://links.lww.com/AOG/D269
2. Evidence Map: http://links.lww.com/AOG/D270

CONFLICT OF INTEREST STATEMENT

All ACOG committee members and authors have submitted a conflict of interest disclosure statement related to this published product. Any potential conflicts have been considered and managed in accordance with ACOG's Conflict of Interest Disclosure Policy. The ACOG policies can be found on acog.org. For products jointly developed with other organizations, conflict of interest disclosures by representatives of the other organizations are addressed by those organizations. The American College of Obstetricians and Gynecologists has neither solicited nor accepted any commercial involvement in the development of the content of this published product.

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