DOI: 10.4274/gulhane.galenos.2024.25348
Gulhane Med J 2025;67(2):67-71

Blind vs. hysteroscopy-guided endometrial biopsy for endometrial pathologies

Şule Atalay Mert, Ahmet Kurt, Tuğba Kınay, Burcu Gündoğdu Öztürk, Hüseyin Levent Keskin

Ankara Etlik City Hospital, Clinic of Obstetrics and Gynecology, Ankara, Türkiye

Cite this article as: Atalay Mert Ş, Kurt A, Kınay T, Gündoğdu Öztürk B, Keskin HL. Blind vs. hysteroscopy-guided endometrial biopsy for endometrial pathologies. Gulhane Med J. 2025;67(2):67-71.

Date submitted:
29.05.2024
Date accepted:
06.11.2024
Epub:
07.05.2025
Publication Date:
03.06.2025

Corresponding Author:
Şule Atalay Mert, M.D., Ankara Etlik City Hospital, Clinic of Obstetrics and Gynecology, Ankara, Türkiye
drsuleatalay@hotmail.com

ORCID:
orcid.org/0000-0002-5711-3933

Keywords: Hysteroscopy guided biopsy, blind biopsy, abnormal uterine bleeding, endometrial thickness, endometrial pathologies

ABSTRACT

Aims: The trend toward minimally invasive methods over basic classical techniques in surgical procedures is rapidly increasing. This study aimed to evaluate the sensitivity of blind biopsy (BB) vs. hysteroscopy-guided biopsy (HGB) for diagnosing malignancy in patients with endometrial pathology.

Methods: This retrospective study included patients who underwent a BB (Group BB) and HGB (Group HGB) because of persistent uterine bleeding or unaltered ultrasonography findings after the initial biopsy at a tertiary facility from October 2022 through July 2023. Patients with a known history of malignancy were excluded. The primary objectives were to compare the performance of the two procedures and calculate a cut-off of endometrial thickness (ET) for a malignancy diagnosis.

Results: The study included 150 patients (mean age: 46.20±11.26 years in Group BB and 46.98±9.77 years in Group HGB, p=0.520). The frequency of endometrial polyps was higher in group BB (61.3% vs. 35.3%, p<0.001), whereas functional endometrium was more frequent in group HGB (41.2% vs. 22%, p<0.001). Mean ET was similar in the two groups (Group BB vs. Group HGB: 11.21±4.96 mm vs. 10.31±5.63 mm, p=0.150). The cut-off of ET in predicting endometrial malignancy was 12.5 mm with a sensitivity of 75% and specificity of 74.6% [area under the curve: 0.775, 95% confidence interval: 0.615-0.935; p=0.009].

Conclusions: The presented study showed no difference between HGB and BB in identifying benign endometrial pathologies. A cut-off of 12.5 mm ET was determined to predict malignancies, though the event rate was low to perform robust calculations.

Introduction

Abnormal uterine bleeding (AUB) is the deviation from the normal menstrual cycle, encompassing changes in the frequency, amount, and duration of menstrual bleeding (1). AUB is a significant gynecological complaint, affecting approximately 30% of women of reproductive age and approximately 70% of the perimenopausal and postmenopausal periods (2). The etiology, diagnosis, and treatment of AUB often involve an endometrial biopsy (EB), a routine procedure in gynecology clinical practice. AUB significantly impairs quality of life and can be effectively treated with methods that offer practical usage advantages, such as the levonorgestrel-releasing intrauterine device. Consequently, non-invasive methods for diagnosing benign endometrial pathologies, such as endometrial polyps causing bleeding, are particularly advantageous (3).

Various methods are employed to evaluate the endometrial pathologies, including blind biopsy (BB) with vabra aspiration, Tao brush, SAP-1 brush sampler, Pipelle, Karman cannula aspiration, and hysteroscopy-guided biopsy (HGB). Endometrial aspiration for histopathological analyses is a safe, minimally invasive, and reliable office endometrial sampling (OES) procedure with minimum discomfort to the patient (4).

Copyright© 2025 The Author. Published by Galenos Publishing House on behalf of University of Health Sciences Türkiye, Gülhane Faculty of Medicine.
This is an open access article under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 (CC BY-NC-ND) International License.

A hysteroscopic biopsy is preferred in conditions like endometrial polyps or fibroids because the biopsy can be performed with direct visualization (5).

Although numerous studies have compared the histopathology results of BB and HGB, their success in diagnosing malignancies and the outcomes of insufficient biopsies need to be evaluated on an individual basis (6). It remains unclear whether HGB is superior to BB in detecting endometrial diseases, endometrial cancer, and endometrial hyperplasia (EH) with or without atypia (7). Therefore, this study examined the biopsy results of BB or HGB in endometrial pathologies and their sensitivity and specificity in diagnosing a malignant disease.

Methods

Design, setting, and study population

This retrospective observational study was conducted at a tertiary gynecology clinic in Türkiye from October 2022 through July 2023. Women aged 30 years who underwent BB or HGB due to endometrial pathology were included. Patients with incomplete records or a history of malignancy, follow-up at another center, or other biopsy techniques such as only pipelle biopsy or sharp curettage were excluded. The study was conducted following the ethical principles outlined in the Declaration of Helsinki, developed by the World Medical Association and adopted in 1964. The study was approved by the Ankara Etlik City Hospital Non-Interventional Clinical Research Ethics Committee (decision number: 546, date: 27/09/2023).

The data was collected using the medical records in the hospital registry. The study hospital uses an established protocol for endometrial pathologies. Women aged 30 years or older with an endometrial pathology [endometrial polyp, postmenopausal bleeding, or postmenopausal endometrial thickness (ET) greater than 4 mm] (8-11) undergo BB with Karman cannula aspiration. HGB is performed in persistent AUB despite EB or when there is no improvement in the initial ultrasonography findings during the 2nd or 3rd-month follow-up after BB.

We divided the patients who underwent a biopsy into two groups. Group BB included patients who underwent blind BB, and Group HGB included patients who underwent HGB because of persistent AUB or no alterations in ultrasonography findings despite BB.

Biopsy procedure

All BBs were performed under local anesthesia via Karman cannula aspiration. The Pipelle was used only in postmenopausal patients or patients with a narrow internal os. All HGBs were performed using a rigid 30-degree optic, 4-mm diameter Ackerman (Eisenbahnstraße 65-67, 78604 Rietheim-Weilheim, Germany) hysteroscope. Fluid distension was achieved using an Endomat (Ackermann HysSurgiSystem, Germany) at a pressure of 150 mm Hg as part of the routine protocol.

Statistical Analysis

All analyses were performed using SPSS software for Windows (version 28.0; IBM Corp, Armonk, NY.). The Shapiro-Wilk test was used to test the normality of the data distribution. Student t-test was used to compare normally distributed variables in the two groups. Non-normally distributed variables were compared using the Chi-square test. Variables were presented as mean ± standard deviation or percentage as appropriate. A p-value of less than 0.05 was considered statistically significant.

Power analysis (G-Power 3.0.0.1) determined that a minimum of 146 cases per group was required to achieve 95% power with a 5% margin of error and an effect size of 0.42 (12).

Results

Sociodemographic findings

The study included three hundred patients. The mean age in Group BB (n=150) and Group HGB was 46.20±11.26 years and 46.98±9.77 years, respectively (p=0.520). Demographic characteristics were similar in the two groups. There were 24.7% (n=37) postmenopausal women subjects in Group BB and 29.3% (n=44) in Group HGB. There was no difference in menopause duration (11.18±7.26 months vs. 11.32±7.80 months, p=0.932) between the two groups. The body mass index (29.26±5.37 kg/m^2 vs. 29.93±4.29 kg/m^2, p=0.230) and obstetric history (gravida, parity, abortion, live children) were similar in the two groups. There was also no between-group difference in ET (11.21±4.96 mm vs. 10.31±5.63 mm, p=0.150) (Table 1).

Histopathological findings

The histopathology results showed no significant differences between the groups in the rates of non-atypical hyperplasia (AH) [2.7% (n=4) vs. 6% (n=9), p=0.156] or malignancy [4% (n=2) vs. 6% (n=8), p=0.054]. No patient was diagnosed with AH. The rate of endometrial polyp was higher in Group BB at 61.3% (n=92) compared to 35.3% (n=53) in Group HGB, with p<0.001. Additionally, functional endometrium was more common in Group HGB at 41.2% (n=61) versus 22% (n=33) in Group BB, with p<0.001 (Table 2).

Patients with a malignancy report

The mean age of patients with malignant biopsy results (MBR) was 65.5±3.54 years in Group BB and 52.5±13.76 years in Group HGB (p=0.035). The rate of MBR was similar in the two groups [5.3% (n=8) vs. 1.3% (n=2)], and all patients with MBR were older than 50 years.

We determined an ET cut-off of the endometrial malignancy diagnosis. Ten patients (3.33%) had a malignancy, including

Table 1. Basic characteristics

	Group BB	Group HGB	p
Age, years, mean ± SD	46.20±11.26	46.98±9.77	0.522
BMI, kg/m²	29.26±5.37	29.93±4.29	0.231
Day of the cycle, mean ± SD	11.7±3.35	12.49±3.79	0.085
Gravidity, mean ± SD	2.76±1.58	3.01±1.47	0.152
Parity, mean ± SD	2.34±1.24	2.61±1.12	0.052
Abortion, mean ± SD	0.40±0.93	0.39±0.77	0.892
Live children, mean ± SD	2.30±1.24	2.56±0.14	0.059
Endometrial thickness, mm, mean ± SD	11.21±4.96	10.31±5.63	0.145
Menopause duration, months, mean ± SD	11.18±7.26	11.32±7.80	0.812
Post-menopausal status, n (%)	44 (29.3%)	37 (24.7%)	0.363
Age of patients with MBR, years, mean ± SD	65.5±3.54 (n=2)	52.5±13.76 (n=8)	0.035

BB: Blind biopsy, HGB: Hysteroscopy-guided biopsy, BMI: Body mass index, MBR: Malignant biopsy result

Table 2. Comparison of histopathology results between the two groups

	Group BB (n=150)	Group HGB (n=150)	p
Endometrial polyp, n (%)	92/150 (61.3)	53 (35.3)	**<0.001***
Non-atypical hyperplasia, n (%)	4/150 (2.7)	9/150 (6)	0.156
Malignancy, n (%)	2/150 (1.3)	8/150 (5.3)	0.054
Functional endometrium, n (%)	40/150 (26.7)	67/150 (44.7)	**<0.001***
Myoma uteri, n (%)	12/150 (8)	13/150 (8.7)	0.835

BB: Blind biopsy, HGB: Hysteroscopy-guided biopsy

endometrial intraepithelial neoplasia and endometrial carcinoma (EC). Nevertheless, the small malignant sample (n=2) size in Group BB made it impossible to perform receiver operating characteristic (ROC) analysis. In Group HGB, ROC analysis was significant for the eight malignancy diagnoses. For the entire population, an ET cut-off of 12.5 mm demonstrated a sensitivity of 75.0% and a specificity of 74.6% in predicting malignancy [area under the curve: 0.775, 95% confidence interval (CI): 0.615-0.935; p=0.009]. The analysis could not determine a relevant cut-off in the premenopausal and postmenopausal women subgroups.

Discussion

This study showed that HGB is not superior to BB in detecting malignancies or other endometrial pathologies. Although there was no difference in malignancy and AH between Group BB and Group HGB, functional endometrial histopathology results were significantly higher in Group HGB.

There is no clear consensus on the techniques for EB to determine the etiology of AUB or increased postmenopausal ET (13). However, in recent years, there has been a growing preference for minimally invasive and cost-effective methods (13). A study comparing direct and flexible hysteroscopy sampling found no difference in the adequacy of tissue samples for diagnosing endometrial pathologies and did not demonstrate the superiority of flexible hysteroscopy (14).

Another study compared preoperative direct hysteroscopic visualization via the grasping technique with the preoperative Novac curette technique to assess the sensitivity of postoperative histopathology (15). The authors compared 121 patients who underwent preoperative blind Novac EB with 129 patients who underwent hysteroscopy. The HGB technique was successful in determining histological tumor type [diagnostic accuracy (0.922 vs. 0.890); k value (0.705 vs. 0.642)] and grade in the presence of endometrioid-type EC (K Cohen 0.354 for G1 and 0.263 for G2 (15). In the presented study, the number of patients diagnosed with MBR was low; 2 of 10 patients with a malignant pathology result were in Group BB (1.3%), and the remaining eight subjects were in Group HGB (5.3%). There was no difference between the groups regarding malignancy, while benign endometrial pathologies were more common in Group BB.

A previous study found that the sensitivity of HGB for diagnosing endometrial polyps ranged from 35.3% to 36.8% when performed at the apex and base of the lesions, while the sensitivity of BB was 29.2% (12). OES had lower diagnostic accuracy for endometrial polyps than surgical polypectomy specimens (12). Pehlivan et al. (16) found higher rates of endometrial polyp

(46.9% vs. 26.5%) and submucous fibroid (4.8% vs. 1.2%) diagnoses in women who underwent hysteroscopy compared to those who underwent probe curettage. In the presented study, endometrial polyp diagnosis was more common in Group BB. A functional endometrium finding was more frequent in Group HGB. Small endometrial polyps removed easily with BB could be the cause of our different findings from previous reports. However, we have no data about the size of endometrial polyps. Researchers need to conduct studies with more detailed data to confirm this assumption.

Various BB techniques exist in gynecology practice (17). Karman cannula aspiration is practical and yields good specimen quality (17). The microscale endometrial sampling biopsy (microscale) is a different minimally invasive technique used to obtain adequate endometrial samples for histopathology, with adequate sampling in 81.2% of subjects (18). Specimen adequacy is associated with age, menopausal status, ET, and endometrial lesion type (18). Additionally, the microscale shows strong agreement with HGB in distinguishing benign and malignant endometrial diseases (kappa 0.950, 95% CI: 0.925-0.975) (17). A study comparing post-hysterectomy AH or EC diagnoses reported a 72% specimen adequacy rate in the direct OES and HGB group (6). On the other hand, HGB improved diagnostic accuracy when preoperative OES was inadequate to determine AH or tumor type and grade. However, when OES yields a diagnosis of grade 1-2 endometrioid tumors, further HGB may provide limited benefits (6). In the current study, the specimen adequacy rate for endometrial polyps, myoma uteri, and malignancy was 73.3% (n=110) in Group BB and 55.3% (n=83) in Group HGB, with no statistically significant difference between the two groups.

In a study evaluating BB results, the most common histopathology report was normal cyclical changes, and malignant lesions were more frequent in patients over 50 (19). In the presented study, compared to the HBG group, the most common histopathology results in the BB group were endometrial polyps and normal cyclical changes. The mean age of patients in both groups diagnosed with MBR was above 50 years. Additionally, the mean age of patients with malignancy diagnosis in the BB group was significantly higher than in the HGB group.

While American College of Obstetricians and Gynecologists does not recommend biopsy for ET less than 4 mm, a thickened endometrium (>4 mm) in a postmenopausal woman with postmenopausal bleeding, detected via transvaginal ultrasonography, warrants further evaluation with endometrial sampling (9). In postmenopausal bleeding, a negative tissue biopsy following “blind” endometrial sampling is not considered a definitive endpoint. Therefore, hysteroscopy is essential to examine the endometrial cavity and rule out focal disease (9). However, studies report different cut-off values for ET. One study reported an optimal cut-off of 8 mm for detecting AH and EC in asymptomatic postmenopausal women, with a sensitivity of 84.6% and specificity of 60.9%. In the current study, the cut-off of ET related to malignant disease was 12.5 mm, with a sensitivity of 75.0% and a specificity of 74.6%. The differing results may be due to the distinct inclusion criteria implemented in the studies. The presented study included all symptomatic women and asymptomatic postmenopausal women with an ET greater than 4 mm.

As a result, many studies have focused on the differences between EB methods. However, a clear cut-off of ET has not yet been established. BB may be the first choice for an effective, non-invasive, and cost-effective EB method for non-malignant endometrial pathologies. When BB fails, HGB may be recommended. In this context, HGB may be preferred for patients over 50 years old and those with suspected malignancy.

This study has several limitations. Due to its retrospective design, maintaining consistent data quality throughout was not possible. Another limitation was the small sample size, which made it difficult to analyze outcomes with low event rates. Additionally, we were unable to compare our findings with hysterectomy results.

Conclusion

This study showed no difference between BB and HGB in detecting malignancy or other endometrial pathologies. It can be concluded that BB should be prioritized as an effective, non-invasive, and cost-effective endometrial biopsy method for non-malignant endometrial pathologies, and HGB can be recommended when BB fails. HGB may be preferred in patients aged >50 years with suspected malignancy.

Ethics

Ethics Committee Approval: The study was approved by the Ankara Etlik City Hospital Non-Interventional Clinical Research Ethics Committee (decision number: 546, date: 27/09/2023).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Ş.A.M., H.L.K., Concept: Ş.A.M., T.K., Design: T.K., B.G.Ö., Data Collection or Processing: A.K., B.G.Ö., Analysis or Interpretation: Ş.A.M., T.K., Literature Search: Ş.A.M., Writing: Ş.A.M., H.L.K.

Conflict of Interest: The authors declared no conflict of interest.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Fraser IS, Critchley HO, Munro MG, Broder M. Can we achieve international agreement on terminologies and definitions used to describe abnormalities of menstrual bleeding? *Hum Reprod.* 2007;22(3):635-643.
2. Goldstein SR, Lumsden MA. Abnormal uterine bleeding in perimenopause. *Climacteric*. 2017;20(5):414-420.
3. Ulubay M, Ozturk M, Firatligil FB, Fidan U, Karaca RE, Yenen MC. Effects of levonorgestrel intrauterine system on patients with female sexual dysfunction. *J Reprod Med*. 2017;62(1-2):26-30.
4. Gupta M, Gupta P, Yadav P, Poonam Y. A randomized comparative study to compare Karman's cannula and pipelle biopsy for evaluation of abnormal uterine bleeding. *J Midlife Health*. 2022;13(1):67-73.
5. Kazandi M, Okmen F, Ergenoglu AM, Yeniel AO, Zeybek B, Zekioglu O, et al. Comparison of the success of histopathological diagnosis with dilatation-curettage and Pipelle endometrial sampling. *J Obstet Gynaecol*. 2012;32(8):790-794.
6. Dueholm M, Hjorth IMD, Dahl K, Ørtoft G. Hysteroscopic resectoscope-directed biopsies and outpatient endometrial sampling for assessment of tumor histology in women with endometrial cancer or atypical hyperplasia. *Eur J Obstet Gynecol Reprod Biol.* 2020;251:173-179.
7. Di Spiezio Sardo A, Saccone G, Carugno J, Pacheco LA, Zizolfi B, Haimovich S, et al. Endometrial biopsy under direct hysteroscopic visualisation versus blind endometrial sampling for the diagnosis of endometrial hyperplasia and cancer: systematic review and meta-analysis. *Facts Views Vis Obgyn*. 2022;14(2):103-110.
8. Timmermans A, Opmeer BC, Khan KS, Bachmann LM, Epstein E, Clark TJ, et al. Endometrial thickness measurement for detecting endometrial cancer in women with postmenopausal bleeding: a systematic review and meta-analysis. *Obstet Gynecol.* 2010;116(1):160-167.
9. Manchanda R, Thapa S. An overview of the main intrauterine pathologies in the postmenopausal period. *Climacteric*. 2020;23(4):384-387.
10. Dijkhuizen FP, Brölmann HA, Potters AE, Bongers MY, Heinz AP. The accuracy of transvaginal ultrasonography in the diagnosis of endometrial abnormalities. *Obstet Gynecol*. 1996;87(3):345-349.
11. Breitkopf DM, Frederickson RA, Snyder RR. Detection of benign endometrial masses by endometrial stripe measurement in premenopausal women. *Obstet Gynecol.* 2004;104(1):120-125.
12. Spadoto-Dias D, Bueloni-Dias FN, Elias LV, Leite NJ, Modotti WP, Lasmar RB, et al. The value of hysteroscopic biopsy in the diagnosis of endometrial polyps. *Womens Health (Lond).* 2016;12(4):412-419.
13. Shen Y, Yang W, Liu J, Zhang Y. Minimally invasive approaches for the early detection of endometrial cancer. *Mol Cancer*. 2023;22(1):53. Erratum in: *Mol Cancer*. 2023;22(1):76.
14. Di Spiezio Sardo A, De Angelis MC, Della Corte L, Carugno J, Zizolfi B, Guadagno E, et al. Should endometrial biopsy under direct hysteroscopic visualization using the grasp technique become the new gold standard for the preoperative evaluation of the patient with endometrial cancer? *Gynecol Oncol*. 2020;158(2):347-353.
15. Breitkopf DM, Hopkins MR, Laughlin-Tommaso SK, Creedon DJ, Famuyide AO. Direct aspiration endometrial biopsy via flexible hysteroscopy. *J Minim Invasive Gynecol.* 2012;19(4):490-493.
16. Agostini A, Shojaï R, Cravello L, Rojat-Habib MC, Roger V, Bretelle F, et al. Endometrial biopsy during outpatient hysteroscopy: evaluation and comparison of two devices. *Eur J Obstet Gynecol Reprod Biol*. 2001;97(2):220-222.
17. Zhang G, Wang Y, Liang XD, Zhou R, Sun XL, Wang JL, et al. Microscale endometrial sampling biopsy in detecting endometrial cancer and atypical hyperplasia in a population of 1551 women: a comparative study with hysteroscopic endometrial biopsy. *Chin Med J (Engl).* 2020;134(2):193-199.
18. Alshdaifat EH, El-Deen Al-Horani SS, Al-Sous MM, Al-Horani S, Sahawneh FE, Sindiani AM. Histopathological pattern of endometrial biopsies in patients with abnormal uterine bleeding in a tertiary referral hospital in Jordan. *Ann Saudi Med.* 2022;42(3):204-213.
19. Pehlivan H, Güler AE, Çakmak B, Atasever M, Bodur S, Kıncı MF, et al. The comparison of two endometrial biopsy techniques in detection of endometrial pathologies. *Ege Tıp Bilimleri Dergisi*. 2019;2(1):26-30.