

Original Article

A Deeper Look at Office Hysteroscopy in Asymptomatic Postmenopausal Patients: Indications and Outcomes of 822 Cases

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ABSTRACT **Study Objective:** This study aims to assess the prevalence of malignancy and other endometrial pathologies in asymptomatic postmenopausal women referred for office hysteroscopy (OH), identify main referral indications, and assess their relationship with the risk of malignancy. Secondary objectives included evaluating the association between ultrasound variables and malignancy risk and assessing procedure validity, which encompasses duration, feasibility, and patient comfort during OH.

Design: Retrospective analysis.

Setting: The study was conducted at the Department of Gynecology, Division of Gynaecology and Obstetrics, University Medical Centre Ljubljana, Slovenia's largest tertiary care center.

Participants: The cohort consisted of 822 asymptomatic postmenopausal women referred for OH, excluding those with postmenopausal bleeding within the last year.

Interventions: Participants underwent OH with or without biopsy.

Measurements and Main Results: The main indication for hysteroscopy was ultrasound abnormalities alone, with remaining indications including a combination of ultrasound and clinical findings. Among the cohort, 97.4% exhibited benign findings, while 2.6% were diagnosed with cancer or precancerous lesions. The analysis revealed that patients with indications based on ultrasound and clinical findings suggestive of malignancy had a higher risk of malignancy compared to those with ultrasound alone. In 387 patients with documented ultrasound variables, inhomogeneous endometrial appearance (OR: 8.2, 95% CI: 2.4–27.9, $p < .001$) and significant liquid content within the uterine cavity (OR: 10.2, 95% CI: 3.6–28.9, $p < .001$) exhibited strong associations with malignancy. Analysis of the procedure revealed a high feasibility rate (87.8%), with a median duration of 13.7 minutes and a median Visual Analog Scale pain score after the procedure of 3/10.

Conclusion: The prevalence of endometrial cancer and precancerous lesions in asymptomatic postmenopausal patients is likely low, with most intrauterine pathologies being benign. Our study demises the utility of routine endometrial surveillance for this population in the absence of specific risk factors. A holistic approach, considering individualized assessments and factors beyond endometrial thickness, is crucial in interpreting ultrasonic findings. *Journal of Minimally Invasive Gynecology* (2025) 32, 258–264. © 2024 AAGL. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>)

Keywords: Hysteroscopy; Uterine lesions; Endometrial cancer; Ultrasound abnormalities; Asymptomatic disease

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Introduction

Hysteroscopy is the gold standard for evaluating intrauterine pathology, particularly crucial in diagnosing and managing conditions within the uterine cavity of postmenopausal patients, where the primary concern is the exclusion of malignancy. Office hysteroscopy (OH), in particular, is favored over inpatient procedures for its minimal invasiveness and avoidance of general anesthesia [1].

Postmenopausal women presenting with bleeding commonly undergo initial assessment through ultrasound and if endometrial thickness exceeds 4 to 5 mm, further evaluation, typically involving OH and biopsy, is recommended [1–3]. Conversely, there are no clear recommendations for the management of women with abnormal ultrasound appearance of the endometrium who do not have bleeding as the indication for their ultrasound. Furthermore, there is no consensus for routine ultrasound assessment in asymptomatic postmenopausal patients without a history of vaginal bleeding. However, in clinical practice, gynecologists occasionally conduct routine ultrasound examinations for asymptomatic postmenopausal patients, during which they may encounter endometrial appearances that arouse suspicion, thus prompting referral for hysteroscopy. Although this practice is frequently observed in countries where gynecologists perform pelvic ultrasounds, it is not widely reported in the literature, and no study has systematically investigated the reasons for referring asymptomatic postmenopausal women for hysteroscopy.

The primary aim of this study was to analyze data on asymptomatic postmenopausal patients referred to our OH clinic, assessing the prevalence of cancer, precancer lesions, and benign findings, while characterizing patient demographics and exploring potential risk factors for malignancy. Specifically, the study sought to identify the main indications for referral to OH and investigate the relationship between these indications and the risk of malignancy. Secondary objectives included evaluating the association between ultrasound variables and the risk of malignancy and assessing OH procedure outcomes.

Methods

Study Design and Setting

This investigation was carried out at the Department of Gynecology, at the Division of Gynaecology and Obstetrics, University Medical Centre Ljubljana, the largest tertiary care center in Slovenia. Notably, a clinical protocol was introduced into regular clinical practice at our institution in 2015, to prospectively monitor and study OH outcomes. This protocol facilitated systematic collection and storage of relevant information in a local database. In 2023, the local Ethical Committee approved the retrospective analysis of prospectively collected data spanning from April 2015 to December 2022.

OH is performed by experienced gynecologist using Betocchi 5.5 or 4.2 mm rigid diagnostic hysteroscopes (Karl Storz, Tuttlingen, Germany) and Truclear 5.2 mm Tissue Removal System (Medtronic, Minneapolis, USA) with a vaginoscopy approach. No pretreatment with NSAIDs or paracervical block is performed before the procedure, but patient are advised to take NSAIDs prior to the procedure, aligning with Level 1 pain management guidelines [4].

Participants

The study cohort comprised individuals drawn from those who were referred for hysteroscopic evaluation at our OH clinic. All the patients had ultrasound examination prior to referral. The inclusion criteria for our analyses comprised being in menopausal status, defined as the absence of menstrual bleeding for at least 12 months, and asymptomatic, defined as no postmenopausal bleeding (PMB) in the previous year.

We only excluded patients who had contraindications for the procedure. In our OH clinic, the procedure is conducted for all patients referred, irrespective of factors like BMI, nulliparity, age, or previous cervical surgery. The only circumstances that represent a contraindication for the procedure in our clinical practice in postmenopausal patients involve suspected active inflammation of the genital tract and cervical tumor obstruction.

Variables

The following data were retrospectively retrieved for each patient: indications for OH based on the primary gynecologist referral, age, age at menopause, years in menopause, BMI, parity, pregnancies, past use of hormonal contraception, history of diabetes, and history of hypertension. Indications for OH were systematically categorized into 4 different groups to facilitate subsequent statistical analyses and interpretation (Table 1).

When reported in the referral for the hysteroscopy, the following ultrasound variables were also recorded: endometrial thickness, maximum polyp length, presence of fluid in the uterine cavity, and appearance of the endometrial echogenicity. Comprehensive data on histology were also obtained, including histological reports for biopsies from OH and subsequent procedures such as surgical inpatient hysteroscopy and dilation and curettage. In cases of hysterectomy, the histological report of the complete specimen was also collected.

Notably, when multiple sampling methods were employed in the same patient, the most clinically relevant histological result was determined based on the following hierarchical order: endometrial cancer (highest grade), atypical hyperplasia, endometrial polyp, cervical polyp, myoma, endometritis, atrophic endometrium, normal endometrium, insufficient tissue.

In instances of multiple histological diagnoses, a singular outcome was allocated to each woman, utilizing the same hierarchy as described above.

Data Sources and Measurement

This investigation utilized data collected prospectively as part of routine clinical practice at the OH clinic and stored electronically in the hospital database. All information was extracted anonymously, ensuring privacy and

Table 1

Categorization of indications for office hysteroscopy

Categories	Variables
Group A—"Ultrasound appearance alone"	One or more of the following: <ul style="list-style-type: none"> – Presence of a polyp – Growing polyp – Thick endometrium – Suspicious endometrium – Mucometra, or hematometra – Presence of a myoma in the uterine cavity
Group B—"Ultrasound + breast cancer with hormonal therapy"	Ultrasound appearance* + being on hormonal therapy for breast cancer
Group C—"Ultrasound + clinical findings suggestive of malignancy"	Ultrasound appearance* + one of the following: <ul style="list-style-type: none"> – Metastases with no origin tumor – Suspicion of paraneoplastic syndrome (eg, pulmonary embolism and deep vein thrombosis) – Sudden weight loss – Previous histology suggestive endometrial abnormalities (eg, papillary projections) – Pathological PAP smear suggesting endometrial origin
Group D—"Other reasons"	One of the following: <ul style="list-style-type: none"> – Patients on hormone replacement therapy without specified ultrasound appearance* – Indication not clearly stated or found in the database

* Ultrasound appearance detailed in group A.

compliance with ethical standards in accordance with the principles outlined in the Declaration of Helsinki. Ultrasound variables, including the thickness of the endometrium or the maximum length of the polyp in millimeters and inhomogeneous appearance of the endometrium, were reported by referring gynecologists and recorded at the time of hysteroscopy. When vacuolization was reported, it was categorized as homogeneous, as this is a well-established feature of a benign polyp. The presence of liquid content in the uterine cavity at the ultrasound was recorded if it was described as copious or as hematometra or mucometra.

Bias

Efforts were made to address potential sources of bias, with a retrospective analysis of otherwise prospectively collected data considered. Although analysis of the reasons for referral does not entirely exclude a selection bias, all the women in the database were referred for hysteroscopy to exclude an intracavitary lesion. The reasons for the lack of histology in patients with unfeasible hysteroscopy procedures were carefully evaluated for each patient.

Statistical Methods

All data were analyzed with SPSS 29.0. Quantitative variables, such as age, BMI, and years in menopause, were handled in statistical analyses. Instances of missing data were accounted for, ensuring that the final analysis reflects an accurate representation of our study population without unjustified exclusions. Statistical analyses involved

Chi-square tests, Student *t* test, logistic regression, and descriptive statistics. The *p*-value was set to .05 as the significance test level.

Results

Demographic Characteristics

Our cohort consisted of 822 asymptomatic postmenopausal women undergoing OH, with a mean age of 63.87 ± 8.15 years. Detailed demographic characteristics are presented in Table 2.

Table 2

General characteristics of study population

Characteristics	Values	Subjects
Age (yrs)	63.9 ± 8.1	(822)*
Age at menopause (yrs)	50 ± 4.3	(802)*
Interval from menopause (yrs)	13.6 ± 8.5	(802)*
BMI (kg/m^2)	29.7 ± 14.1	(713)*
Chronic hypertension	351 (42.7%)	(822)*
Diabetes	67 (8.2%)	(822)*
Past use of hormonal contraception	426 (51%)	(822)*
	Parity	
Pregnancies	2 (0–11)	(810)*
Deliveries	2 (0–11)	(810)*

Skewed data are expressed as medians (range); normal data are expressed as means \pm SD.

* Different number of cases due to missing data.

Histological Outcomes

The final histopathological outcomes of the 822 patients are listed in Table 3. Out of the total cases, 21 cases (2.6%) were identified with cancer or precancer lesions, while most patients (97.4%) had benign lesions or a benign appearance on hysteroscopy that did not necessitate further evaluation. Endometrial polyps were most common (62%), followed by atrophic endometrium (5.6%), cervical polyp (3.2%), and myoma (1.1%). Malignant cases included serous carcinoma (4 cases), clear cell carcinoma, mesonephric-like carcinoma, and gastrointestinal mucinous carcinoma (1 case each).

Notably, 24.0% of cases did not have a biopsy performed during OH nor with other procedures (“No histology available”). In most of these cases, a diagnostic hysteroscopy was conducted, but an endometrial sample was not deemed necessary by the clinicians. For the remaining cases in this group, lack of histology was attributed to other reasons which are presented in the section “OH Outcomes” of this article.

Indications for Hysteroscopy

A significant finding was that patients referred for OH due to clinical concerns indicative of malignancy were diagnosed with cancer in 36.8% of the cases. In contrast, patients that were referred for ultrasound findings alone (81.0% of cases) had malignancy in only 2%. The statistical analysis demonstrated a significant correlation between the referral reasons and the detection of malignancy (Pearson Chi-square 92.655, $p < .001$), as shown in Table 4.

Table 3

Histopathological outcomes of 822 asymptomatic postmenopausal patients referred to office hysteroscopy sorted by frequency

Pathology	822 (100)
Benign findings	801 (97.4%)
Endometrial polyp	510 (62%)
No biopsy taken	197 (24%)
Benign appearance at OH	125 (15.2%)
Procedure aborted with follow-up not recommended	55 (6.7%)
Lost to follow-up without visualization of the cavity	17 (2.1%)
Atrophic endometrium	46 (5.6%)
Cervical polyp	26 (3.2%)
Myoma	9 (1.1%)
Normal endometrium	7 (0.9%)
Insufficient tissue	5 (0.5%)
Endometritis	1 (0.1%)
EC and AH	21 (2.6%)
Endometrial cancer nonaggressive histological type*	12 (1.4%)
Endometrial cancer aggressive histological type*	7 (1%)
Atypical hyperplasia	2 (0.2)

EC = endometrial cancer; AH = atypical hyperplasia.

* According to “FIGO staging of endometrial cancer: 2023” [5].

Table 4

Association of indications for hysteroscopy with presence of malignancy

Indications	Benign	EC and AH
US alone ($N = 666$)	653 (98.0%)	13 (2%)
US + Breast cancer with hormonal therapy ($N = 96$)	95 (99.0%)	1 (1.0%)
US + Clinical findings suggestive of malignancy ($N = 19$)	12 (63.2%)	7 (36.8%)
Other reasons ($N = 41$)	41 (100.0%)	0 (0.0%)

AH = atypical hyperplasia; EC = endometrial cancer; US = ultrasound.

Clinical and Ultrasound Variables

No significant associations were found between malignancy and variables such as age, BMI, high blood pressure, past use of hormonal contraception, or nulliparity (Table 5). In contrast, diabetes emerged as a significant risk factor ($p = .008$).

There were no significant differences in endometrial thickness or polyp length between cases with and without malignancy. However, an inhomogeneous endometrial appearance and the presence of conspicuous intracavitary fluid were significantly associated with malignancy ($p < .001$) (Table 6).

OH Outcomes

In our study, OH was attempted in all 822 cases and was successfully performed in 719 cases (87.5%). Among the feasible procedures, the breakdown of each procedure was as follows: diagnostic hysteroscopy (176), biopsy (165), polypectomy (373), myomectomy (3), and adhesiolysis (2).

However, in 103 cases (12.5%), OH was deemed not feasible mostly due to pain intolerance and cervical stenosis.

Table 5

General characteristics of the two study groups and their significance

	Benign	EC and AH	p
Age (yrs)	63.8 ± 8.0	66.7 ± 11.5	.099*
Age at menopause (yrs)	50.3 ± 4.4	50.0 ± 5.5	.733*
Interval from menopause (yrs)	13.5 ± 8.4	15.7 ± 9.2	.254*
BMI (kg/m^2)	29.7 ± 14.2	28.2 ± 4.2	.657*
Chronic hypertension	343 (42.8%)	8 (38%)	.666†
Diabetes	62 (7.7%)	5 (23.8%)	.008†
Past use of hormonal contraception	88 (10.9%)	5 (23.8%)	.137†
Nulliparity	78 (9.8%)	3 (15%)	.968†

AH = atypical hyperplasia; EC = endometrial cancer.

* Student *t* test.

† Pearson Chi-square.

Table 6

Associations of the ultrasound variables with malignant histological diagnosis

Ultrasound variables	Benign	EC and AH	p	OR (95% CI)
Endometrial thickness (<i>N</i> = 223)*	12.6 ± 8.6 (214) [†]	11.2 ± 9 (9) [†]	.625 [§]	
Length of polyp (<i>N</i> = 171)*	18.4 ± 8.5 (166) [†]	18.6 ± 5 (5) [†]	.973 [§]	
Inhomogeneous appearance (<i>N</i> = 387)*	48 (12.7%) [‡]	6 (54.5%) [‡]	.002 [§]	8.2 (2.4–27.9)
Presence of conspicuous intercavitary fluid (<i>N</i> = 412)*	23 (5.8%) [‡]	7 (38.8%) [‡]	<.001 [§]	10.2 (3.6–28.9)

95% CI = confidence interval; AH = atypical hyperplasia; EC = endometrial cancer.

* Number of patients for which the ultrasound variables was reported.

[†] Means ± SD in millimeters (number of cases with data on ultrasound variables).[‡] Frequencies and percentages within histology categories.[§] Pearson Chi-square.

Detailed examination of these cases revealed that in three instances, a cervical polyp was removed even though access to the uterine cavity was not possible. In other 55 of these cases, no clinical indication for further investigation was identified following the unsuccessful attempt at hysteroscopy. For the remaining 45 cases, additional procedures (repeat OH, inpatient surgical hysteroscopy, or D&C) were deemed necessary and scheduled. Seventeen of these 45 patients scheduled for further procedures, did not attend their scheduled follow-up.

Data on the duration of the procedure were available for 811 patients. The mean procedure duration was mean 13.7 minutes (SDs 8.7). Among the 668 patients who provided pain scores using the Visual Analog Scale (0–10), the median score reported was 3 (IQR: 2–4).

Discussion

Main Findings

Our analysis of 822 asymptomatic postmenopausal women assessed through OH identified a low prevalence (2.6%) of cancerous and precancerous lesions, predominantly identifying benign endometrial polyps. This study stands out as the first to systematically examine and report the indications for OH in this population, revealing that although most patients are referred for an ultrasound finding, cancer was mostly diagnosed in those patients who also presented with clinical concerns indicative of malignancy. Crucially, the analysis of the ultrasound indications highlighted that inhomogeneous endometrial appearance and conspicuous intracavitary fluid were markedly associated with malignancy while the endometrial thickness or size of polyp were not.

Results in Context and Clinical Implications

While dedicated analyses on the prevalence of endometrial cancer in this specific demographic are difficult to

obtain, our findings suggest that in asymptomatic women, the prevalence of cancerous and precancerous lesions remains significantly lower than in women with PMB. This aligns with other studies focusing on asymptomatic populations, which have reported varied prevalence rates, spanning from 1.2% to 5.1%, but generally support the notion that the absence of PMB correlates with a lower likelihood of significant pathology [6–14]. Accordingly, the guidelines from American, European, and Canadian societies converge on the consensus that routine endometrial surveillance in asymptomatic postmenopausal patients, even those on tamoxifen, is not recommended [2,15–17]. Contrary to these guidelines, the literature has predominantly focused on endometrial thickening as a potential indicator of endometrial cancer in asymptomatic patients [18]. To the point where a recent meta-analysis, raising controversy, suggested that a cut-off of 3.0 mm could justify further endometrial evaluation [19–21]. Our research, instead, by delving into the referral reasons for OH, offers two novel perspectives on risk assessment and management.

First, that relying solely on ultrasound may lead to unnecessary interventions, as evidenced by the observed low prevalence of malignancy in this group (Table 4). This means that while ultrasound remains a valuable diagnostic tool, its interpretation should be complemented by a holistic evaluation of the patient's clinical history and risk factors.

Secondly, our analyses shows that the inadequacy of ultrasound alone is mostly related to the poor predictive value of endometrial thickness (p-value = .625) and it points to consider other sonographic features.

The International Endometrial Tumor Analysis (IETA) group has significantly contributed to this subject by emphasizing that a thickened endometrium is associated not only with cancer but more frequently with benign pathologies like endometrial polyps or hyperplasia without atypia [9]. On the other hand, the IETA-1 and IETA-3 studies demonstrated that an endometrium with malignant or premalignant pathology often exhibited nonuniform echogenicity, in both symptomatic

and asymptomatic women [9,22,23]. Intense vascularity was also shown to be of importance, but it was not evaluated in our study due to poor information on vascularity in the ultrasound data.

While the association between intracavitary fluid and endometrial cancer was first recognized in a landmark study in 1982, the subsequent work by Goldstein in 1990, “Look at the doughnut rather than the hole,” was responsible for shifting the focus toward endometrial thickness [24–26]. This was mainly due to the fact that even a normal atrophic postmenopausal endometrium, when combined with cervical stenosis, can result in endometrial fluid collections [27]. Consequently, in our study, terms like hematometra or mucometra were used to indicate a large amount of intracavitary fluid, while a small amount was deemed negative. The significant correlation between abundant intracavitary fluid and cancer, found in our study, reignites this discussion suggesting that malignant lesions likely lead to increased fluid collection. A limitation of our study, however, is the lack of data regarding fluid quantity. Future research should investigate a cutoff value for endometrial cavity fluid volume, using the measurement recommendation of the IETA group, to better explore its relationship with malignancy [28].

Lastly, our study gives important consideration on the feasibility of OH in this population. In 822 cases, hysteroscopy was successfully carried out in 87.4% of instances. This aligns with existing literature, such as Sauvan et al. [29], which reported a success rate of 76.4% for OH in postmenopausal women. It is also noteworthy that although we found a low median Visual Analog Scale, a few patients reported a high pain score of 9.

Despite low complication rates and the advantage of an OH, considering its feasibility and possible discomfort of the patient, we think that a careful evaluation of its necessity in each clinical scenario is indispensable.

Strength and Limitations

Our study benefits from several strengths that enhance the robustness of our findings. With a considerable cohort of 822 asymptomatic postmenopausal patients, our investigation stands as one of the larger studies within this specific demographic. Notably, the application of less stringent exclusion criteria for the OH procedure enabled us to capture the full spectrum of asymptomatic postmenopausal women. Moreover, we collected and analyzed diverse clinical data allowing for a thorough exploration of associations and patterns. Importantly, the data were originally collected prospectively, mitigating the risks associated with retrospective analyses and enhancing the reliability of our dataset.

However, it is imperative to acknowledge certain limitations that provide context for the scope and implications of our study. The single-center nature of our research may limit the generalizability of findings to broader populations

or varied healthcare settings. Additionally, given that our study involved patients referred for OH, there exists a potential selection bias, limiting the representation of the entire asymptomatic postmenopausal population, particularly those who do not seek gynecological evaluation.

A critical consideration is the potential for recall bias, as our study relies on patients’ recollections of abnormal bleeding. Lastly, the retrospective design introduces inherent limitations related to the consistency of documentation. While efforts were made to extract data accurately, variations in documentation practices may influence the completeness and accuracy of our dataset, which is especially relevant for ultrasound data.

Conclusions

This study reaffirms the low prevalence of endometrial cancer and precancerous lesions in asymptomatic postmenopausal women, advocating for selective referrals to OH based on nuanced clinical evaluations and specific ultrasound characteristics. Future research should aim to refine surveillance strategies for endometrial thickening detected on ultrasound and further investigate other ultrasound parameters such as endometrial homogeneity and the significance of intracavitary fluid. Our findings highlight the importance of tailored diagnostic approaches to enhance patient care and underscore the need for continued exploration in this critical area of women’s health.

Declaration of competing interest

The authors declare that they have no conflicts of interest in connection with this manuscript.

IRB Approval

This study was approved by the Slovene Committee for Medical Ethics on October 17, 2023. Approval number: 0120-265/2023/3.

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