

Trends in Hysteroscopic Endometrial Sampling in Women 70 Years or Older

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Abstract

Objective: To characterize office and operating room hysteroscopy in women 70 years of age or older. **Design:** This was a retrospective chart analysis. **Setting:** A single tertiary-care medical center. **Population:** All women aged 70 years of age or older who underwent a hysteroscopy procedure between March 2011 and August 2018. **Methods:** All hysteroscopic interventions performed during the study period were reviewed. All patients had at least one gynecological examination that included an ultrasound study prior to the hysteroscopy. **Main outcome measures:** Primary outcomes included procedure success and histopathological findings. Secondary outcomes included short-term complications of the procedure. **Results:** The data of 577 patients were analyzed. The median age at the time of the procedure was 76 years. 225 office hysteroscopy procedures and 405 operating room procedures were included. Of the 236 patients with PMB, 73(30.9%) were diagnosed as having malignancy compared to 25 (7.3%) of the 341 patients with no PMB ($p < .001$, odds ratio (OR) = 5.66; confidence interval (CI) 3.46-9.26). The office procedure was successful in 194 (87%) patients. 53 patients required a second hysteroscopy, which revealed 12 cases of premalignant or malignant lesions. The volume of procedures in the office increased 16 times during the study period. **Conclusions:** Office hysteroscopy for women over the age of 70 is safe, feasible, and reliable for diagnosis of endometrial malignancy. Failed hysteroscopy and a moderate-to-high index of suspicion for malignancy indicates the need for a repeat hysteroscopy. The diagnostic yield using the office procedure has increased over time.

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Keywords: endometrial cancer, endometrial hyperplasia, general anesthesia, menopause, office hysteroscopy.

Introduction

Abnormal uterine bleeding, suspected endometrial polyps, and endometrial thickness are sources of concern among postmenopausal women and require tissue biopsy of the endometrial finding.^{1,2} Advancements in technique and miniaturized instruments have made it possible to combine diagnostic and operative hysteroscopy in an outpatient setting without anesthesia (the “see-and-treat” technique). This technique, which offers numerous advantages and has gained increasing popularity in recent years, is particularly relevant to postmenopausal women, due to the higher rates of comorbidities and higher risks associated with anesthesia in this age group.

We previously evaluated the accuracy of outpatient hysteroscopy among peri- and postmenopausal women and showed it to be an adequate and reliable tool mainly for the evaluation of benign pathology, with a sensitivity of 93.1%, a specificity of 52.1%, a positive predictive value of 90.4%, and a negative predictive value of 61% for a visual diagnosis of any pathology³.

The present study focused on women 70 years and older, given the combination of higher risks of anesthesia and the higher rates of clinically significant findings in that group. The aim of this study is to characterize both office hysteroscopy and operating room (OR) hysteroscopy for the diagnosis of endometrial pathologies. In addition, we aimed to illustrate trends in the utility of hysteroscopy techniques and in the yield of abnormal findings in this age group over a period of 7 years.

Methods

Study Population

This study was approved by the Research Ethics Committee at the Tel Aviv Sourasky Medical Center (0749-15-TLV on 10.11.2016). We used the data on all consecutive women 70 years of age or older who were referred to our medical center for a hysteroscopy procedure between March 2011 and August 2018. Patients

in the office hysteroscopy group were retrieved from the hysteroscopy clinic's medical charts, and patients in the OR hysteroscopy group were identified according to their OR diagnosis (ICD codes 68.12 and 68.16). All hysteroscopic interventions that had been performed during the study period were reviewed, including repeat hysteroscopies for the same patient. Cases of repeat hysteroscopic procedures for the same patient that were not related to her primary procedure were excluded from the analysis. All the patients referred to either office or OR hysteroscopy had undergone at least one gynecological examination that included an ultrasound study before their referral to our unit.

Women were assigned to the postmenopausal bleeding (PMB) group if they presented with PMB, regardless of ultrasonographic findings. Women who were referred due to any ultrasound finding with no PMB were assigned to the abnormal sonographic findings group.

The "see-and-treat" technique was implemented in our institution with the opening of a new outpatient hysteroscopy clinic in 2011, and a change of clinical practice of referring women to the office instead of directly to the OR as a first-line procedure was gradually introduced in our medical community.

Procedures

Office procedures were performed without anesthesia. The surgeon used narrow caliber hysteroscopes, i.e., a 3.8 mm telescope with a 30-degree oblique lens and a 5-Fr working channel (compact hysteroscope; Richard Wolf GmbH, Knittlingen Germany), a 1.9 mm scope with a 3 mm diagnostic sheath (Mini-Hysteroscopes, Olympus Corporation, Hamburg, Germany) and a 1.8 mm telescope with 3.5 mm diagnostic sheaths with a 5F operative canal (Alphascope; Gynecare, division of Ethicon, Inc., Somerville, NJ). Illumination was provided by a high-intensity cold-light source via a fiberoptic lead. The uterine cavity was distended with normal saline infused by a pressure bag at a pressure of 50-100 mmHg. The vaginoscopic approach was used in all cases. Polypectomy was performed with a bipolar coaxial electrode (Gynecare VersaPoint, Ethicon Inc., Somerville, NJ). Endometrial biopsies were performed by means of a bipolar electrode, flexible scissors, or grasping forceps. All procedures were performed by two gynecologists (SB and GR).

OR procedures were performed under anesthesia and by mean of either a 3.8 mm telescope with a 30-degree oblique lens and a 5Fr working channel (compact hysteroscope; Richard Wolf GmbH, Knittlingen, Germany) or a Versapoint 2 bipolar resectoscope 24Fr (J&J, Germany). The uterine cavity was distended with a Stortz Endomat Select hysteroscopy fluid management system set to a pressure of approximately 100 mmHg.

Hysteroscopy was defined as successful only if penetration through the cervical internal os was achieved and the entire uterine cavity was visualized. Hysteroscopy was defined as failure when no penetration of the uterine cavity was achieved. It was defined as incomplete when the surgeon could not complete the procedure in one step, e.g., partial resection of an endometrial polyp for which additional office or OR procedures were usually recommended. Incomplete procedures were counted among the successful procedures.

Data were collected by reviewing the computerized medical records with a de-identified pre-prepared data sheet. All of the study patients' computerized records were searched for follow-up information until the end of the study period.

Statistical Analysis

Nominal data were described as numbers and percentages. Continuous data were assessed for normal distribution (Shapiro-Wilk test) and provided as the mean \pm standard deviation or median (P₂₅-P₇₅). Quantitative data were analyzed with the chi-square or Fisher exact test. Continuous variables were compared between groups by means of the t-test or the Mann-Whitney nonparametric test, as appropriate. All statistical tests were 2 sided, with $p < 0.05$ considered statistically significant. Data analyses were conducted with the Statistical Package for the Social Sciences, version 25.0 (IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp) and Microsoft Excel version 14.0 (Microsoft Corporation, Redmond, Washington).

Results

A total of 642 hysteroscopies for 577 patients aged 70 years or older were performed during the study period. The median patient age at the time of the procedure was 76 years (interquartile range [IQR] 73-80). Two-hundred and thirty hysteroscopies were performed in the outpatient hysteroscopy clinic, and 412 hysteroscopies were performed in the OR. Twelve patients underwent repeat hysteroscopic procedures unrelated to the primary procedure, and those repeat procedures were excluded from the analysis. The final analysis consisted of a total of 630 hysteroscopies, of which 225 were performed in the office and 405 in the OR. Five-hundred seventy-seven hysteroscopies were first interventions and another 53 were second interventions. Two-hundred and twenty-two of the former patients were included in the office hysteroscopy group, and 355 patients were included in the OR hysteroscopy group.

Figure 1A illustrates the volume of procedures among the two groups of women during the study period. While the total number of hysteroscopies more than doubled during this period, the number of procedures for this population in the outpatient hysteroscopy clinic increased by approximately 16 times. Thus, by the end of the follow-up period, an office procedure became the primary hysteroscopic intervention for patients 70 years of age or older.

The study population included 416 (72.1%) patients aged 70-79 years, 155 (26.9%) patients aged 80-89 years, and six (1.0%) patients aged 90 years and over (the oldest was 93 years old). The baseline characteristics of the two groups are detailed in **Table 1**. The median age at the time of hysteroscopy was 76 years (IQR 73-80), and it was similar for the two groups. More women were referred to office procedures due to abnormal sonographic findings (67.1% vs. 49.6%, $p < 0.001$: Table 1), while more women with active PMB were referred to procedures in the OR (47% vs. 31.1% $p < 0.001$: Table 1).

The procedure was successful in 194 (87.4%) patients whose procedure was performed in the office compared with 342 (96.3%) patients whose procedure was performed in the OR under anesthesia. The diagnosis of cervical stenosis or difficulty in penetrating the cervix was significantly higher in the office group. Out of 54 (24.3%) cases in the office group with cervical stenosis, the surgeon managed to enter the uterine cavity in 32 (59.2%). The surgeon failed to penetrate the uterine cavity, mainly due to cervical stenosis, obstructive cervical mass, and patient intolerance, in 28 (12.6%) of office hysteroscopies. Forty-five (20.3%) of the hysteroscopies in our clinic were not completed in a one-step procedure, mainly due to large or multiple findings and uterine bleeding. Only 7 (3.15%) procedures were abandoned due to patient discomfort.

A total of 47 (21.2%) patients who underwent office hysteroscopy required a second hysteroscopy, 19 due to failure in the first visit, 27 due to incomplete procedures, and one due to continuous bleeding that precluded the performance of the intervention. In 44 of those 47 cases, the second hysteroscopy was performed in the OR under general anesthesia. A total of six patients who underwent OR hysteroscopy under general anesthesia required a second procedure (two cases due to failure and four cases due to non-diagnostic histopathologic samples taken at the first procedure).

Overall, 150 (67.6%) of office hysteroscopies had a positive finding. Moreover, 43 (43/69=62.3%) of the women with PMB and 106 (106/149=71.1%) of those with abnormal sonographic findings also had a positive hysteroscopic finding(s). The histopathological findings by groups are shown in **Table 2**. PMB was a risk factor for malignancy for the entire cohort, with 73/236 (30.9%) patients with PMB diagnosed as having a malignancy compared to 25/341 (7.3%) patients with no PMB ($p < .001$, odds ratio (OR) = 5.66; confidence interval (CI) 3.46-9.26). In the repeat hysteroscopy subgroup, 7/17 (41.2%) patients with PMB were diagnosed as having a malignancy compared to 6/36 (16.7%) patients with no bleeding ($p = .053$, odds ratio (OR) = 3.5; confidence interval (CI) 0.95-12.89).

Figure 1B illustrates the relative contribution of each of the hysteroscopic approaches to the diagnosis of new abnormal findings among the 577 patients included in our cohort.

While samples taken in the outpatient hysteroscopy clinic during the first years did not contribute to a new diagnosis, their contribution increased during the following years.

All patients who underwent hysteroscopy in our outpatient clinic were discharged on the same day. The

median length of hospitalization was three days (range 0-28 days) for the patients who underwent the procedures in the OR. Three-hundred and twenty-nine cases (92.7% of all procedures under anesthesia) were performed in an inpatient setting, while 26 (7.3% of all procedures under anesthesia) were performed in our outpatient ORs.

Short-term complications among patients treated in our outpatient hysteroscopy clinic included one case (0.45%) of uterine perforation that was managed expectantly, and one case of bleeding that necessitated admission a few days later for a repeat procedure under general anesthesia. Four of the 355 (1.13%) patients who underwent an OR hysteroscopy sustained uterine perforation. Emergent abdominal surgeries were required in three of those cases, and they included two abdominal hysterectomies, including one case of left colectomy. Three patients (0.85%) sustained complications that required admission to the intensive care unit (ICU): there was one cardiac arrest, and two cases of severe sepsis (secondary to pyometra). Unfortunately, the latter two patients died during the hospitalization, yielding a mortality risk of 0.56% for patients aged 70 years or older in our cohort who underwent OR hysteroscopy.

Discussion

Decisions concerning any procedure under general anesthesia are less easily made due to the associated comorbidities and higher risks among women older than 70 years of age. The performance of a procedure in the OR may also be affected by the unwillingness of the patient to undergo general anesthesia when given the option, even at the cost of not reaching a diagnosis.

Altogether, 194 (87.4%) patients in our cohort who were referred to office hysteroscopy had a successful procedure. Our results showed a success rate similar to the 74.5% success rate for office hysteroscopy in postmenopausal women recently reported by Sauvan et al⁴. Sousa et al., who used a hysteroscopic technique similar to ours on 88 postmenopausal patients with genital bleeding, reported similar failure rates of 17.8%⁵.

Endometrial sampling was generally less likely to be performed in the office compared to the OR, but the fact that more than one-half of the women in our cohort (58.6%) did have a biopsy taken during the office procedure is of considerable diagnostic value for this age group. It is important to emphasize that even incomplete procedures, which were much more common in the office group than in the OR group, are of some value in this age group, especially if a biopsy has been carried out. For example, if a biopsy from a benign endometrial polyp is taken, the patient and her physician would feel more confident about choosing a conservative sonographic follow-up, thus avoiding a procedure under anesthesia. With good medical practice becoming more and more tailored to the individual needs of the patient, we should be aware of this option for minimizing risks to the patient.

Bleeding and large or multiple findings were a leading cause of failed or incomplete procedures in the office, while in the OR they limited the procedure in only two cases. Bleeding in the uterine cavity limits the operating viewing field during hysteroscopy, but this problem is overcome in the OR by washing the uterine cavity continuously with an irrigation flow pump using higher pressures than those used in the office. This also serves to explain the significant difference in the indications for which women were referred to the treatment options. More women were referred to office procedures due to abnormal sonographic findings, while more women with active PMB were referred to procedures in the OR.

Our results revealed that cervical stenosis is not a contraindication for office hysteroscopy. We managed to overcome cervical stenosis in more than half of the patients who presented with it (32/54 cases, 59%). The techniques used in our clinic to contend with cervical stenosis are either mechanical, including forcing pressure with the hysteroscope or using scissors, or electrical by means of a bipolar electrode for widening the orifice and penetrating through the fibrotic tissue. Pretreatment with 25 mcg of vaginal estradiol in combination with 400 mcg of vaginal misoprostol before the procedure can facilitate passage of the hysteroscope through the cervical canal⁶.

Malignancy was found in 30.9% of the patients who presented with PMB, as well as in 7.3% of the patients who had no PMB. The pathological results from the repeat hysteroscopy are striking. One-quarter (12/48) of

the samples retrieved from repeat hysteroscopy were abnormal. This emphasizes the importance of pursuing a diagnosis. In selected cases of a moderate-to-high index of suspicion, we do not favor a conservative sonographic follow-up but rather recommend referring the patient directly to a repeat hysteroscopy. It is noteworthy that malignancy was detected in 6/36 (16.7%) of the patients who did not present with PMB and who were referred to a repeat hysteroscopy.

The volume of procedures in the office increased 16 times during the study period, and a higher percentage of malignancies was diagnosed compared to office procedures (**Figure 1B**). These trends are the result of a newly implemented technique in our institution, and also of a change of clinical practice of referring women to the office option as a first-line procedure. Once the refined biopsy-taking technique was implemented, no significant change in yield was observed during the last three years of the study, indicating that the technique is relatively quickly and easily learned and put into practice.

The most compelling advantage of office hysteroscopy compared to OR hysteroscopy in this cohort is the absence of complications in the former and the rate and severity of complications in the latter, including ICU hospitalization, sepsis, abdominal operation, and two mortalities related to the OR hysteroscopy procedure. A similar recent publication on office hysteroscopy in postmenopausal women also did not observe any complications, such as uterine infection, uterine perforation, or genital tract hemorrhage⁴.

Our study has several limitations. The main limitation is that the two sub-groups were not matched for demographic and clinical characteristics or for indications for undergoing the procedure. Also, we did not have information on previous procedures that may have been performed outside our medical center. It is likely that some patients with a history of failure of a previous trial of office procedures were directly referred to OR hysteroscopy. While our data are primarily descriptive, they nevertheless suggest that office hysteroscopy for women over the age of 70 is safe, feasible, and reliable. Moreover, to the best of our knowledge, this is the first study to compare office and OR hysteroscopy for this age group. We believe that patient selection will improve with greater application of office hysteroscopy and as more and more physicians become aware of its advantages as well as its limitations. This, in turn, will lead to higher rates of successfully completed procedures and to higher rates of accurate pathological diagnoses in the office setting. Further prospective trials are needed in order to confirm our findings. Such studies may help to design a tool for better patient selection for either office or OR hysteroscopy.

Conclusions

The technologies currently available for office-based hysteroscopy are advantageous for patients 70 years of age or older in order to avoid the risks of anesthesia and to promote lower complication rates and fair chances of a complete procedure. In patients with failed hysteroscopy and a moderate-to-high index of suspicion of malignancy, a repeat hysteroscopy is recommended. Trends over time have enabled the achievement of significant numbers of pathological diagnoses in the office, making the office procedure a viable option, especially for a patient population characterized by higher rates of clinically significant findings.

Contributors

S.B.O and D.G conceived of the presented idea and study design. N.S and A.B.D collected the data and analyzed it. D.G, S.B.O and N.S oversaw data collection and statistical analysis. S.B.O. and D.G wrote the manuscript with input from N.S, G.R and A.B.D.

Declaration of interests

S.B.O, N.S, G.R, A.B.D and D.G have nothing to disclose.

Ethical approval statement:

This study was approved by the Research Ethics Committee at the Tel Aviv Sourasky Medical Center (0749-15-TLV on 10.11.2016).

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TABLE 1 Preoperative and operative characteristics

Variable

Age, years, median (IQR)

Indications for hysteroscopy Post-menopausal bleeding, n (%) Abnormal sonographic findings ^a, n (%) Other indications ^b,

Successful procedure, n (%)

Incomplete procedure, n (%)

Main findings during procedure Endometrial polyp, n (%) Thickened endometrium, n (%) Atrophic endometrium, n (%) Su

Main types of intervention Total operative hysteroscopy, n (%)

Hysteroscopic polypectomy, n (%)

Hysteroscopic myomectomy, n (%)

Tissue sampling, n (%)

Removal of IUD, n (%)

Main reasons for failure or incomplete procedure Cervical stenosis, n (%)

Pain or intolerance, n (%)

Large/multiple findings or bleeding, n (%)

Uterine perforation, n (%)

Other failure ^c, n (%)

OR, operative room; *IQR*, *interquartile range* ^a Including 5 mm or more thickened endometrium, suspected endometrial pol

TABLE 2 Histopathologic findings

Variable

Tissue sampling during procedure, n (%)

Histologic report, n (%) **Benign** Abnormal Premalignant ^a Malignant ^b **Non-diagnostic**

^a Including hyperplasia or complex hyperplasia without atypia (n = 13), metaplasia/hyperplasia/complex hyperplasia with

FIGURE LEGEND

Figure 1. Trends in the utility of hysteroscopy techniques and the occurrence of abnormal findings for women 70 years and older during the study period

- A. The annual volume of activity according to the type of procedure
- B. The annual diagnosis of abnormal findings according to the type of procedure (%)

* According to data collected until August 31, 2018.

Second hysteroscopy - hysteroscopy performed after failed or incomplete office hysteroscopy

