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Research Article

# The Value of Hysteroscopy in the Diagnosis of Endometrial Cancer

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**Abstract**

**Introduction:** Endometrial cancer is the most common malignancy of the female genital tract in developed countries. Hysteroscopy allows direct visualization of the uterine cavity and has the capacity of detecting malignant pathologies such as endometrial cancer, and it permits an endometrial sampling or removal of the lesion during the same procedure.

**Objective:** To evaluate the efficiency of outpatient hysteroscopy for the diagnosis of intrauterine pathology.

**Material and Methods:** Retrospective study with 891 outpatient hystesocopies performing and eye-directed biopsy, according to the hospital protocol. Patients were divided into four diagnostic categories for the endometrium classification; normal, benign pathology, suspected hyperplasia or suspected malignancy.

**Results:** 26 patients were diagnosed of endometrial cancer with the histologic study, 24 of them suspected on hysteroscopy (92.3%). The mean age was 65.27, being 88.5% of patients postmenopausal. The most common symptom was Postmenopausal Bleeding (PMB) present in the 86.9% of the postmenopausal patients. All the patients had abnormal findings in the Transvaginal Ultrasound (TVUS).

**Conclusion:** Hysteroscopic view presents excellent specificity for endometrial cancer (99.1%) and good sensitivity for endometrial cancer (92.3%).

**Keywords:** Endometrial cancer; Hysteroscopy; Diagnosis; Sensitivity

## Abbreviations

AUB: Abnormal Uterine Bleeding; TVUS: Transvaginal Ultrasonography; ET: Endometrial Thickness; PMB: Postmenopausal Bleeding; D&C: Dilatation and Curettage

## Introduction

Endometrial cancer is the most common malignancy of the female genital tract in developed countries, and the second in mortality after ovarian cancer [1]. For the last 30 years there has been an increase in the number of diagnoses. Its incidence is rising among pre and postmenopausal women; every year, about 200.000 new endometrial cancers are diagnosed around the world and an estimated 50.000 women die from this illness [2].

The risk of endometrial cancer is positively correlated with the excessive endometrial stimulation with estrogen, associated with older age, early menarche, late menopause, nulliparity, obesity, family history of endometrial cancer, Polycystic Ovarian Syndrome, as well as hormone replacement therapy [3]. Other risk factors include personal history of breast cancer and genetic predisposition (Lynch syndrome) [4]. Diabetes, hypertension, and geographical and socioeconomic factors are still inconclusive [5].

The most common symptom of endometrial cancer is Abnormal Uterine Bleeding (AUB). However, up to 20% of patients can be asymptomatic at the time of diagnosis [7]. For all stages taken together, the overall 5-year survival is around 80% [8].

The most important prognostic features for endometrial cancer are the stage (FIGO), the myometrial infiltration, histological type and differentiation grade [9].

The Transvaginal Ultrasonography (TVUS) has been the first-line diagnostic test to detect endometrial pathology. It shows endometrial thickness and heterogeneous variations within the echogenicity of the endometrium [10]. Because of its non-invasive nature and its high accuracy, it is used extensively to assess the endometrium.

The cut-off value for Endometrial Thickness (ET) in asymptomatic women is not well established [11,12]. The most frequently used optimal threshold level of endometrial thickness measure to separate postmenopausal patients into low-risk and high-risk patients is 4-5mm [11].

Some authors suggest that an endometrial thickness cut-off

**Table 1:** Suspected cases with endometrial neoplasia correlated with histological examination.

| | Endometrial carcinoma |
|---|---|
| **Suspected endometrial carcinoma on hysteroscopic view** | 24 |
| **Histologic diagnosis of endometrial carcinoma** | 26 |
| **False positive** | 0 |
| **False negative** | 2 |




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**Table 2:** Patient's age and symptomatology, echography suspicion and malignancy during hysteroscopy, as well as the anatomopathological result of the endometrial biopsy performed during hysteroscopy and post-surgical stage.

| | Age | Symptoms | TVUS | Hysteroscopy suspected malignancy | Anatomopathologic study | FIGO stage |
|---|---|---|---|---|---|---|
| **1** | 58 | PMB | ET > 5mm | Yes | Endometrioid adenocarcinoma G1 | IA |
| **2** | 39 | Intense dysmenorrhoea | ET > 5mm | Yes | Endometrioid adenocarcinoma G1 | IA |
| **3** | 64 | PMB | ET > 5mm | Yes | Endometrioid adenocarcinoma G1 | IA |
| **4** | 77 | PMB | Endocavitari mass | No | Endometrioid adenocarcinoma G1 | IA |
| **5** | 69 | PMB | ET > 5mm | Yes | Undifferentiated carcinoma | IIIC1 |
| **6** | 59 | PMB | Endocavitari mass | Yes | Endometrioid adenocarcinoma G1 | IA |
| **7** | 68 | PMB | Endocavitari mass | No | Endometrioid adenocarcinoma G2 | IA |
| **8** | 68 | Asymptomatic | ET > 5mm | Yes | Endometrioid adenocarcinoma G1 | IA |
| **9** | 84 | PMB | ET > 5mm | Yes | Carcinosarcoma | IA |
| **10** | 61 | PMB | Endocavitari mass | Yes | Endometrioid adenocarcinoma G1 | IIB |
| **11** | 55 | PMB | ET > 5mm | Yes | Endometrioid adenocarcinoma G2 | IA |
| **12** | 73 | PMB | Ovarian tumor | Yes | Endometrioid adenocarcinoma G3 | IIIB |
| **13** | 50 | Bleeding between menstrual periods | ET > 5mm | Yes | Endometrioid adenocarcinoma G1 | IA |
| **14** | 62 | Asymptomatic | Endocavitari mass | Yes | Papillary serous carcinoma | IIIC2 |
| **15** | 72 | PMB | Endocavitari mass | Yes | Undifferentiated carcinoma | IVB |
| **16** | 60 | PMB | Endocavitari mass | Yes | Papillary serous carcinoma | IA |
| **17** | 82 | PMB | Endocavitari mass | Yes | Papillary serous carcinoma | IVB |
| **18** | 71 | PMB | ET > 5mm | Yes | Endometrioid adenocarcinoma G1 | IA |
| **19** | 52 | PMB | ET > 5mm | Yes | Endometrioid adenocarcinoma G3 | IB |
| **20** | 66 | PMB | Endocavitari mass | Yes | Carcinosarcoma | IVB |
| **21** | 67 | PMB | Endocavitari mass | Yes | Endometrioid adenocarcinoma G1 | IIIB |
| **22** | 73 | PMB | ET > 5mm | Yes | Leiomyosarcoma | IA |
| **23** | 51 | Heavy menstrual bleeding | ET > 5mm | Yes | Endometrioid adenocarcinoma G1 | IIIA |
| **24** | 65 | Asymptomatic | ET > 5mm | Yes | Papillary serous carcinoma | IA |
| **25** | 62 | PMB | ET > 5mm | Yes | Papillary serous carcinoma | |
| **26** | 92 | PMB | * | Yes | Papillary serous carcinoma | IVB |

TVUS: Transvaginal Ultrasound; PMB: Postmenopausal Bleeding; ET: Endometrial Thickness
*No data on the TVUS of this patient.

value of 10mm does not miss any cases of endometrial cancer [13,14]. Therefore, the hysteroscopy examination and the sequential endometrial biopsy for the histopathological examination of tissue are essential to get an endometrial carcinoma diagnosis.

Hysteroscopy allows direct visualization of the uterine cavity. In most cases, it detects malignant pathologies and, in these circumstances, it permits an endometrial sampling or removal of the lesion during the same procedure [15,16].

Although the final diagnosis is histologic, there are some morphological hysteroscopic criteria that are indicative of endometrial cancer. The purpose of this study is to evaluate the diagnostic accuracy of hysteroscopy for de diagnosis of malignant endometrial lesions.

## Objective

To evaluate the efficiency of outpatient hysteroscopy for the diagnosis of intrauterine pathology.

## Materials and Methods

The study was a retrospective diagnostic-type test. It involves 891 outpatient hysteroscopies performed between July 2012 and December 2015 in the department of Obstetrics and Gynaecology of Igualada Hospital.

Each patient underwent an outpatient hysteroscopy with no anaesthesia and no cervical or endometrial rispering pre-intervention, according to the hospital protocol. The procedure was carried out by two experienced hysteroscopists using one of two hysteroscopic systems (the Truclear 5.0 Tissue Removal System or the Versapoint Bipolar Electrosurgery System). All the procedure involved an eye-directed biopsy in which a standard forceps with a polyp grip was used for extracting intrauterine tissue.

With the hysteroscopic reports, patients were divided into three diagnostic categories for the endometrium classification; normal, benign pathology and suspected malignancy.

The objective of this study was to assess the accuracy of hysteroscopy and endometrial biopsy in the diagnostic of endometrial malignancy.

For statistical analysis, the sensitivity, specificity, positive predictive value and negative predictive value were analyzed.

## Results

A total of 26 patients with histologic diagnoses of endometrial cancer were investigated, to whom a hysteroscopy was performed. Among them, the hysteroscopic examiner suspected endometrial cancer in 24 cases (Table 1).

There were two cases of false negatives in which the examiner described the hysteroscopic image as large polyps. The anatomopathological study showed focus of endometrioid carcinoma grade 1 and 2, the first one above the polyp.

In the 26 patients with the histologic diagnosis of endometrial carcinoma, the 88.5% were postmenopausal. The mean age was 65.27 (range 39-92).

The most common symptom was Postmenopausal Bleeding (PMB) present in the 86.9% of the postmenopausal patients. Three of the postmenopausal patients were asymptomatic, who underwent a TVUS for genital prolapse study, suspecting endometrial pathology that required hysteroscopic study.

In patients of reproductive age (3/26), the most common form of presentation was menstrual disturbances as heavy menstrual bleeding (33.3%) and bleeding between menstrual periods (33.3%). The third pre-menopausal patient presented intense dysmenorrhea, and was diagnosed of synchronous ovarian neoplasm.

All the patients had abnormal findings in the TVUS, described as endocavitari mass (40.0%), endometrial thickness > 5mm in menopausal women (56.0 %) and synchronous ovarian neoplasm (4.0%).

Among the most frequent personal history, the highlights are hypertension (13/26), obesity (6/26), diabetes mellitus (7/26), dyslipidaemia (7/26) and psychiatric disorders such as depression (6/26). None of the patients were undergoing treatment with tamoxifen or hormone replacement therapy.

The most common type of cancer was endometrioid adenocarcinoma (50%) (Table 2) with histologic subtypes G1 (42.3%), G2 (7.9%) and G3 (7.9%). After the post-surgical staging, most of the cases correspond to stage IA [14] in the FIGO classification. The more advanced stages correspond to more aggressive histologic subtypes; IVB for undifferentiated carcinoma, papillary serous carcinoma and carcinosarcoma. However, in the endometrioid carcinomas there are also some cases of advanced stages, less frequently than in the most aggressive histological subtypes. Only 5 out of 15 endometrioid carcinomas were not an IA stage in the FIGO classification.

In our study, we obtained a sensitivity of 92.3% with hysteroscopy for the diagnosis of endometrial cancer and it presents excellent specificity (Table 3). The final diagnosis was reached with pathological study sample obtained during hysteroscopy.

**Table 3:** Sensitivity, specificity, positive and negative predictive values for diagnosis of endometrial cancer on hysteroscopic view.

| | Presence of endometrial carcinoma (%) |
|---|---|
| **Sensitivity** | 92.3 (24/26) |
| **Specificity** | 99.1 (857/865) |
| **Positive predictive value** | 75.0 (24/32) |
| **Negative predictive value** | 99.7 (857/859) |

## Discussion

In our study, for the assessment of endometrial carcinoma, hysteroscopy has high diagnostic accuracy with sensitivity of 92.3%, specificity of 99.1%, positive predictive value of 75.0% and negative predictive value of 99.7%. Previous studies showed that hysteroscopy is an accurate diagnostic method to discriminate between normal and pathologic endocavitary conditions in both symptomatic and asymptomatic women, with values ranging from 85% to 98% [17]. In addition, hysteroscopy has the capability of reducing sampling errors, very common in blind Dilatation and Curettage (D&C) technique, which can miss focal pathology or endometrial precancerous lesions [18].

Many studies have described hysteroscopic features of neoplastic morphology [19-21] and one group conducted a study to develop a systematic score system for identification of endometrial cancer [22]. Despite the higher accuracy of the score system compared with subjective evaluation of the endometrium, it must be evaluated in larger populations and not selected patients in order to generalize its use.

However, performing an eye-directed biopsy during the hysteroscopy has been shown to be the best strategy, not only to diagnose a neoplasm but to accurately differentiate benign pathology such as endometrial polyps from pre-cancerous lesions like endometrial hyperplasia [15,23].

Although it has been shown that the best test to study the endometrial pathology is hysteroscopy, usually the endometrial study begins with a TVUS. Sonographic measurement of endometrial thickness is an accurate and easy procedure to determine whether further investigations are needed to rule out malignancy. Different cut off values for endometrial thickness have been used, but guidelines recommend a cut-off value of 3 to 5mm below which endometrial cancer is unlikely in symptomatic women [24,25]. This limit is not well established in asymptomatic women in whom an endometrial thickness of up to 10mm could be normal.

Despite the high sensibility of transvaginal ultrasound to diagnose intrauterine disorders, endometrial thickness or Doppler ultrasonography measured by transvaginal ultrasonography has low specificity for predicting malignant endometrial disorders [16,26].

The literature support that the combined use of ultrasonography and hysteroscopy, with eye directed biopsy, is the most appropriate diagnostic strategy for not infradiagnosticating endometrial pathology such as cancer [27]. The importance of hysteroscopy is also shown in the present study, in which 92.3% of the cases of endometrial cancer were suspected by hysteroscopy and confirmed with eye-directed biopsy on histologic examination. On two occasions, the neoplasm

was not suspected and the hysteroscopist reported endometrial polyps. These two patients had presented a post-menopausal bleeding and had undergone an ultrasound to study if there was endometrial pathology, which also suspected benign pathology.

Therefore, it is important to study all post-menopausal metrorrhagia, because it is usually the main clinical sign of endometrial carcinoma. The prevalence of this symptom in endometrial carcinoma-afflicted patients highlights the need to study these patients to rule out endometrial pathology. This fact is also evident in our sample, where 88.5% of patients are post-menopausal and the most frequent symptom within these was post-menopausal bleeding. For these reasons, hysteroscopy should be considered in all women with postmenopausal uterine bleeding due to the increased risk of endometrial carcinoma within this group [27,28].

On the other hand, asymptomatic patients with suspected endometrial pathology by TVUS can't be despised. In the sample of the present study, it is observed that asymptomatic patients may have high-grade histologic subtypes such as papillary serous carcinoma and present with advanced stage carcinoma. At the same time, it is important not to forget the premenopausal patients, poorly rethought in the study sample (3/26), age group in which the incidence of endometrial carcinoma is increasing. It is thought that that the increase of endometrial carcinoma in younger women is due to an early onset of obesity [3]. In the current study, obesity, along with other pathologies carried out with the metabolic syndrome, are widely present as concomitant diseases of the patients.

## Conclusion

Hysteroscopic view presents excellent specificity for endometrial cancer (99.1%) and good sensitivity for endometrial cancer (92.3%). Despite the good validity of hysteroscopic view, biopsy is essential for endometrial hyperplasia and cancer diagnosis.

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