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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. Outpatient hysteroscopy is a minimally invasive technique which allows the complete evaluation of uterine cavity. On the other hand, during the diagnostic procedure, the specialist has the possibility of taking an endometrial sampling for histological study. The aim of the present study is evaluating the efficacy of outpatient hysteroscopy for the diagnosis of intrauterine pathology.

Material and Methods: A retrospective survey that includes 891 patients who were subjected to an outpatient hysteroscopy and an eye-directed biopsy during the same procedure. Socio-demographic data were collected. Depending on the hysteroscopic diagnosis made by the specialist, the patients were divided into three diagnostic categories; no pathology, benign pathology or suspected malignancy.

Results: 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%. All the patients had abnormal findings in the transvaginal ultrasound (TVUS). In 26 patients; the histologic study showed the diagnosis of endometrial cancer, in 24 of them the hysteroscopy suspected malignancy (92.3%).

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 [6-8].

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) is the gold standard for the diagnosis of 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 as the first line endometrial diagnosis. Currently, the cut-off value for Endometrial Thickness (ET) in asymptomatic women is not well established [11,12] yet.

Some authors suggest that an endometrial thickness cut-off 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 and examination of the uterine cavity. In some cases, it can also suspect malignant pathologies and, in these circumstances, hysteroscopy allows to perform an endometrial sampling or removal of the endometrial pathology in an outpatient setting 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 assess the diagnostic accuracy of hysteroscopy and endometrial biopsy in the diagnosis of malignant

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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

endometrial lesions.

Material and Methods

A retrospective study was carried out in which a total of 891 patients with outpatient hysteroscopy were included. The hysteroscopy was performed between July 2012 and December 2015 in Igualada's Hospital.

The procedures were carried out in ambulatory care with no anesthesia or sedation of any sort. No cervical or endometrial preparation was performed pre-intervention.

The procedure was conducted by two experienced hysteroscopists (MDB, JRP) using one of the two hysteroscopic systems (the Truclear 5.0 Tissue Removal System (Smith & Nephew) with mechanical energy or the Versapoint Bipolar Electro surgery System (Gynecare; Ethicon Inc.) with bipolar energy).

All the procedure involved a systematic examination of the uterine cavity and an endometrial eye-directed biopsy in the suspected pathology, or at random if we had not suspicion of any pathology. The 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: no pathology, benign pathology and suspected malignancy.

Other variables were assessed: Socio-demographic data and obstetrician antecedents (parity: Nulliparous, 1 delivery, vaginal *vs.* cesarean; hormonal status: menopause *vs.* no menopause).

Statistical analysis: for statistical analysis, we have provided a general description of the variables included in the study (sensitivity, specificity, positive predictive value, and negative predictive value).

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

S.No	Age	Symptoms	TVUS	Hysteroscopy suspected malignancy	Anatomopathologic study	FIGO stage
1	58	PMB	ET > 5mm	Yes	Endometrioid adenocarcinoma G1	IA
2	39	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	Spotting	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	Hypermenorrhea	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

Results

Of the total outpatient hysteroscopy that was carried out, we obtained a total of 26 patients with histologic diagnoses of endometrial cancer. Among them, the hysteroscopic examiner suspected endometrial cancer in 24 cases (Table 1 and Table 2). There were two cases of false negatives in which the examiner described the hysteroscopic image as large polyps. The other patients were classified in the category no pathology (n=452) and benign pathology (n=415).

The mean age of these patients was 65.27 (range 39-92), and 88.5% were postmenopausal. Table 3 shows the clinical, echography and hysteroscopy variables, and anatomopathologic results of 26 patients with diagnosis of endometrial carcinoma.

Among the most frequent personal history, the highlights are hypertension (13/26), obesity (6/26), diabetes mellitus (7/26), dyslipedemia (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%) with histologic subtypes G1 (42.3%). However, in the endometrioid carcinomas there are also some cases of advanced stages, less frequent 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

The hysteroscopy is an accurate diagnostic method to discriminate between normal and pathologic endocavitary conditions in both symptomatic and asymptomatic women [17]. In the current study, for the assessment of endometrial carcinoma, hysteroscopy has obtained a sensitivity of 92.3%, a specificity of 99.1%, a positive predictive value of 75.0%, and a negative predictive value of 99.7%. 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 to 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 5 mm 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 supports 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, neither by the hysteroscopy nor the ultrasound study which suspected endometrial polyps. It must be highlighted that the anatomopathological study showed focus of endometrioid carcinoma in the polyp, and in these cases, have a suspect that can be more complicated for the specialist.

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 our study sample (3/26), but with an incidence of endometrial carcinoma increasing [3].

Conclusions

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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