# Diagnostic performance of Cornier' pipelle endometrial biopsy in comparison with dilatation and uterine curettage

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*Abstract*

***Objective.*** *The main objective of the study was to determine the reliability of the Cornier' pipelle endometrial biopsy in determining endometrial cancer, and the comparison of this with the gold standard method, dilatation and curettage.* ***Materials and methods.*** *A number of 105 patients with indication of endometrial biopsy were included in this study. Initially the Cornier' pipelle endometrial biopsy was achieved, followed immediately by dilatation and curettage. It was measure the insertion failure rate of the water gauge, the rate of the inadequacy specimen for histological assessment, agreement of histophatological results between the two methods, patients comfort and associated complications.* ***Results and discussions.*** *The mean age of the patients included in the study was 53.8 years (SD 10,4; between 30 to 80 years). Majority of the patients were post-menopausal (54%) the rest of 30% being in perimenopausal period. In 9 cases (8,6%) from post-menopausal patients with cervical stenosis, Cornier's pipelle water gauce could not be introduced into the uterine cavity than only after cervical dilatation and in 7 cases (6.7%) the Cornier's pipelle method did not obtain sufficient material for histological examination. Kappa coeficient of 0.61 (p<.001) showed a substantial to moderate line between the two methods. Cornier's pipelle endometrial biopsy detected 14 cases of endometrial cancer from 16, and in two cases was diagnosed complex hyperplasia with endometrium atypia, with suspicious invasion areas. Cornier's pipelle sensibility method was 92.3% for simple hyperplasia, 61.5% for polyps and 59.4% for benign pathology of the endometrium.* ***Conclusions.*** *The Cornier's pipelle method caused less pain than uterin curettage at patients taken in the study. In the cases in which this method cannot be used or the obtained sample is failure, it is recommended an additional evaluation of the patients. Cornier's pipelle method is reliable, precise and convenient for detecting endometrial cancer, the sensibility of this being modest in diagnosis of benign pathology of the endometrium.*

***Keywords:*** *curretage, biopsy, endometrium, cancer*

## Introduction

Abnormal uterine bleeding is an important symptom of both benign and malignant gynecological disease. Potential causes of abnormal bleeding could include neoplasias, hormonal dysfunctions, reproductive tract trauma, infections, coagulopathies and complications of pregnancy. As a consequence, abnormal uterine bleeding is one of the most frequent symptoms in gynecology, affecting women of all age. Abnormal uterine bleeding affects 10 to 30% women of reproductive age and in the order of 50% of those in perimenopause[1,2,3,4].

Abnormal uterine bleeding in women aged 35 and older, especially in postmenopause, requires evaluation, first of all to exclude hyperplasia and cancer of the endometrium, but also to identify the underlying pathology and choose the appropriate treatment for the patient[5]. Most of the clinical algorithms for the management of patients with abnormal uterine bleeding are focused on the identification of endometrial cancer. Early diagnosis of endometrial cancer is almost entirely dependent on the prompt recognition and evaluation of irregular bleeding. Abnormal bleeding in premenopausal women is not a reason for concern from the cancer point of view, as there is a wide range of potentially physiologic causes, the incidence of uterine cancer under the age of 40 being very small[6,7]. However, postmenopausal metrorrhagy is particularly worrisome and requires evaluation as the likelihood of diagnosing endometrial cancer is 5-10%[8,9]. In patients with abnormal bleeding, biopsy end histopathological evaluation of the endometrium can reveal infections or neoplastic lesions such as endometrial hyperplasia, cancer, polyps or gestational trophoblastic neoplasia, the traditional gold standard being represented by dilatation and uterine curettage. In the 1970s, metallic vacuum-suction and curettage devices allowed sampling of the endometrial without anesthesia in an office setting. Among these, the most popular was the Vabra aspirator, which was 86% accurate in diagnosing of endometrial cancer[10,11]. Subsequently,

cheaper, smaller, less painful plastic catheters with their own internal pistons to generate suction became popular. The Cornier' pipelle device is one of the most reliable samplers, which has similar efficacy when compared to Vabra[12,13]. This method had some advantages like: an outer sheath of 23.5 cm in length and 3.1 mm in diameter with a distal aperture (2.4 mm in diameter) in the side of the cannula through which the endometrial specimen is aspirated[5]. However, Cornier' pipelle endometrial biopsy has several important limitations. In approximately 10% of cases the obtained material is insufficient for histopathological examination, a problem occurring especially in postmenopausal patients, where up to 68% of samples were reported to be inadequate[14]. It has been shown that the percentage of endometrial surface sampled by the Cornier' pipelle device is only 4%[15]. A meta-analysis evaluating the performance of several suction biopsy devices found the Cornier' pipelle sampler to be the most reliable and accurate, with a sensitivity of 99.6% and 91% in postmenopause and premenopause, respectively[16]. In spite of all these, the sensitivity of endometrial Cornier' pipelle biopsy is considerably variable in the literature. In some studies, the endometrial cancer diagnosis has been failed between 7.6 and 32.4%[17,18,19,20,21]. From these data it is shown that Cornier' pipelle endometrial biopsy could present erroneous results, especially in the cases in which the pathology is not global but rather focal (polyps, focal hyperplasia or carcinoma localized to a small area of the endometrium).

The present study follow the setting of the diagnostic performance of Cornier' pipelle sampler and comparing it to gold standard, dilatation and uterine curettage, aiming the insertion failure rate, inadequacy of tissue rate for histopathological evaluation, patient comfort and associated complications.

## Material and methods

Of the patients presenting to the 1st Obstetrics and Gynecology Clinic from Târgu-Mureş, over a period of 1 year, with the indication of endometrial biopsy, 105 cases were included in this study. Before performing the procedures an informed consent was signed by the patients. After a detailed clinical assessment including history, gynecological examination and transvaginal ultrasonography, patients were prepared in a usual way for dilatation and uterine curettage. Initially the Cornier' pipelle endometrial biopsy was performed without anesthesia or dilatation, followed immediately by dilatation and uterine curettage, using 1% xyline solution as local anesthetic. Tissue samples obtained by the two methods were introduced in formaldehyde 10% solution, sent to the pathologic laboratory and embedded in paraffin. About 3-4 μm sections were cut, mounted, dewaxed and stained with hematoxylin and eosin. Histopathological samples were interpreted by the same pathologist, without knowledge of the previous procedures, not to influence the interpretation. It was measured: the insertion failure rate, tissue inadequacy for histopathological examination, the line between histopathology results of Cornier' pipelle biopsy and gold standard, patient comfort and associated complications. The inability to introduce the Cornier' pipelle device in the uterine cavity without cervical dilatation from three attempts represented the failure of the procedure. Adequacy of the material was defined as at least one endometrial sample large enough to determine the gland-to-stroma ratio and the morphological features of the endometrium. For the statistical analysis, SPSS 14.0 and McNemar's chi-square test (with the continuity correction) were used to compare the result of successful endometrial biopsies between the two methods. The level of line between the two histophatological results was measured by Cohen's Kappa coefficient, with values of 0.40-0.59 (moderate), 0.60-0.79 (substantial) and 0.80-1 (outstanding). For the Cornier' pipelle versus the "gold standard", sensitivity, specificity, positive and negative predictive values and likelihood ratio were calculated. Histopathology results from the hysterectomy specimens were compared with uterine curettage results for determination of final histophatological gold standard results. To compare endometrial thickness at successful Cornier' pipelle biopsies, we used the Mann-Whitney U test. Patient comfort was evaluated with a visual analogue pain scale completed by the patient at the end of the procedures, and compared using the non-parametric Wilcoxon test.

## Results and discussion

The mean age of the patients included in the study was 53.8 years (SD 10.4; range between 30 and 80). The majority of patients were postmenopausal (54%), the other 30% being the women in perimenopausal. The indications for endometrial biopsy were: postmenopausal bleeding (47%), pre- and perimenopausal bleeding (26%), uterine leiomyomas with metrorrhagia/pre-hysterctomy biopsy (18%), endometrial echographic lesion or abnormal cytology (9%). The most frequent complaint was irregular bleeding (74%), followed by severe acute bleeding (13%) and menorrhagia (6%).

In 9 cases (8.6%) from postmenopausal patients with cervical stricture, the Cornier' pipelle device could be introduced in the uterine cavity only after cervical dilatation. In an outpatient setting this would have meant the failure of the method. Uterine curettage failed in a single patient with a very fibrous and heavy cervix, where the Pipelle obtained adequate sample for examination. In 7 cases (6.7%), after being correctly introduced in the uterine cavity, the Cornier' pipelle technique failed to obtain sufficient material for histopathological examination, while uterine curettage was unable to

obtain adequate material in 2 cases (1.9%), being statistically insignificant (p = .125). Endometrial thickness measured on transvaginal ultrasound in these cases was between 6 and 21 mm.

The mean endometrial thickness measured before intervention in patients where Cornier' pipelle technique was unable to obtain an adequate sample was 10.1 mm (SD 5.6; min. 6- max. 21), and 12 mm (SD 7.3; min.- 2 max. 40) in patients where sampling was sufficient, showing a statistically insignificant difference between the two groups (p = .652).

Histopathology result obtained by the Cornier' pipelle technique agreed with those obtained by curettage in 64 cases from 96 (66.7%) (table 1). Calculated Kappa value of 0.61 (p< .001) showed substantial to moderate line between the two methods.

The sensitivity, specificity, positive and negative predictive values and likelihood ratio for the Cornier' pipelle method is shown in table 2. Global sensitivity of Cornier' pipelle technique in postmenopause and premenopause was 68% and 65.2%, respectively (p = .77).

The Cornier' pipelle device detected 14 cases of endometrial cancer from 16, in 2 cases diagnosing complex atypical hyperplasia of the endometrium with suspicious areas of invasion. Thus, the sensitivity and specificity of Cornier' pipelle technique in detecting endometrial cancer was 87.5% and 100%, respectively. If considering that atypical hyperplasia of the endometrium with suspicion areas of invasion is identical to the diagnosis of malignancy until proven otherwise, sensitivity and specificity of Cornier' pipelle device in detecting endometrial cancers were 100%. Histopatholgical cancer types detected in this study are shown in Table 3. In the case of using Cornier' pipelle technique, the detecting of atypical hyperplasia of the endometrium or simple hyperplasia was failed. In endometrial benign histophatology settings, the sensibility of Cornier' pipelle technique was only 59.4% and 61.5% in polyps detection. Using uterine curettage it was missed one case of endometrial adenocarcinoma, which was detected by Cornier' pipelle and, subsequently, also confirmed by the hysterectomy specimen.

*Table 1* Histopatholgy results obtained by the two biopsy methods: Cornier' pipelle and uterine curettage

| Histopathological type of the endometrium | Histopathology results | |
|---|---|---|
| | Gold standard (uterine curettage) No. | Cornier' pipelle in line with the „gold standard" No. (%) |
| Proliferative | 15 | 7 (46.7) |
| Secretory | 4 | 1 (25) |
| Menstrual | 7 | 5 (71.4) |
| Glandular and stromal collapse | 6 | 3 (50) |
| Atrophy | 7 | 6 (85.7) |
| Endometritis | 1 | 0 |
| Polyp | 26 | 16 (61.5) |
| Simple hyperplasia | 13 | 12 (92.3) |
| Atypical hyperplasia | 1 | 0 |
| Cancer | 16 | 14-16* (87.5-100)* |
| **Total** | **96** | **64-66* (66.7-68.8)*** |

** in two cases of endometrioid endometrial adenocarcinoma, Cornier' pipelle biopsy diagnosed complex atypical hyperplasia of the endometrium with suspicious areas of invasion*

A percent of 88.4% from patients experienced no pain or only slight discomfort with the Cornier' pipelle procedure, as compared to the uterine curettage group (p .<001) which in 81% of cases caused moderate to unbearable pain. No uterine perforation or any other complications were noticed during the study.

The main reason for performing endometrial biopsy in patients with abnormal uterine bleeding is to confirm the benign nature of the disease and to exclude cancer, allowing optimal management to be implemented through medical treatment or conservative surgery. The traditional "gold standard" method of endometrial evaluation represented by dilatation and uterine curettage, is one of the most frequent interventions performed in gynecology[22]. Widespread use of this technique was criticized for many years, leading to the introduction of many alternative sampling techniques for the detection of endometrial pathology[23], the most popular of these being the Cornier' pipelle sampler, which when compared to the gold standard, was easy to use, faster, and cost-effective[24].

Gordon and Westgate[13] have been showed that the failure insertion values are between 1.2% and 3%, and the inadequate sample proportion between 1% and 16%[21,23,25]. Our data by using Cornier' pipelle technique is not in line with these results, the failure insertion values being much higher (8.6%).

In all the patients, where the Cornier' pipelle device could not be introduced through the cervix, were postmenopausal, cervical stenosis being much more frequent in this age group. From 7 patients where the Cornier' pipelle technique did not obtain suffici-

**Table 2** Accuracy of Cornier' pipelle biopsy in determining the endometrium histopathology

| Histopathological type of the endometrium | Sens.[1] | Spec.[2] | PPV[3] | NPV[4] | LR[5] |
|---|---|---|---|---|---|
| Benign | 59.4 | 90.6 | 76 | 81.7 | 6.33 |
| Atrophy | 85.7 | 95.5 | 60 | 98.8 | 19.07 |
| Polyp | 61.5 | 87.14 | 64 | 85.9 | 4.786 |
| Simple hyperplasia | 92.3 | 91.6 | 63.1 | 98.7 | 10.95 |
| Cancer | 87.5-100* | 100 | 100 | 97.6-100* | - |

** in two cases of endometrioid endometrial adenocarcinoma, Cornier' pipelle biopsy diagnosed complex atypical hyperplasia of the endometrium with suspicious areas of invasion; 1. sensitivity, 2. specificity, 3. positive predictive value, 4. negative predictive value, 5. likelihood ratio*

**Table 3** Histopathological endometrial cancer types detected by Cornier' pipelle technique

| Histopathological type of endometrium cancer | No. |
|---|---|
| Complex atypical hyperplasia of the endometrium with suspicious areas for invasion | 2 |
| Endometrioid type adenocarcinoma of the endometrium | 11 |
| Endometrial clear cell adenocarcinoma | 1 |
| Malignant mixed mullerian tumor (carcinosarcoma) | 1 |
| Keratinizing squamous cell carcinoma of the cervix with infiltrate endometrium | 1 |
| **Total** | **16** |

ent material after being correctly introduced in the uterine cavity, 5 were postmenopausal. Totalizing the cases of failed insertion with the ones where the Cornier' pipelle device did not obtain sufficient tissue for examination, results that in an outpatient setting the Cornier' pipelle method would have failed in obtaining a histopathology result in 15.2% of cases, which is less then reported by others[14,23,26].

Elsandabesee and Greenwood[19] have shown that there is only a 27% probability of obtaining an adequate endometrial sample if the central endometrial thickness is less than 5 mm. This study didn't succeed to show a correlation between endometrial thickness and failure of the method, being in line with the study of the two authors.

In the present study, the global sensitivity of the Cornier' pipelle technique was only 68.8%, which is much lower as compared to the results reported by Stovall (96-98%)[27].

The sensitivity, specificity, positive and negative predictive values of the Cornier' pipelle method for the detection of endometrial cancer were 87.5%, 100%, 100% and 97.6%. In the literature, detection rates of endometrial cancer with the Cornier' pipelle device vary between 67% and 98%[18,19], while preoperative biopsy had 99.2% sensitivity at patients with high grade of endometrial tumors, showing a high sensitivity[28,29].

In our study also, the Cornier' pipelle method successfully detected malign endometrial tumors of non-endometrioid type, carcinosarcoma and keratinizing squamous cell carcinoma with endometrial invasion.

It was diagnosed a single case of complex atypical hyperplasia of the endometrium using the uterine curettage, which was missed by the Cornier' pipelle technique. Cornier' pipelle sampling also failed to detect a single case of simple hyperplasia without atypia from 13. However, in benign pathology it showed a modest sensitivity, detecting until 61.5% of endometrial polyps and 85.7% of endometrial atrophies. Furthermore, only 59.4% was correctly diagnosed from benign disease cases, these differences having, however, only minimal clinical significance. Consequently, Cornier' pipelle technique is a reliable method for diagnosis of cancers and simple hyperplasia of the endometrium, but modest for detecting polyps or other benign lesions.

## Conclusions

Cornier' pipelle technique is a reliable and accurate method in detecting endometrial cancer of any histopathological type. Diagnosis of endometrial cancer in an outpatient setting will expedite the appropriate treatment, saving considerable financial resources. When this technique can't be used, or the obtained tissue is inadequate, further evaluation of the patients is required. ■

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