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Research Article

# The diagnostic value of endometrial cytology in diagnosing endometrial pathology

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## Summary

Endometrial carcinoma remains one of the leading places in terms of frequency among oncogynecological diseases, both in countries with developed primary and secondary prevention and in countries with poorly functioning prevention. The implementation of screening programs would lead to the detection of oncological diseases in outpatient settings at an early stage, which would lead to positive socio-economical effects for society. This study aims to determine the test's validity through the following criteria: sensitivity, specificity, and negative and positive predictive value of endometrial cytology compared with the histological result of examined tissue samples. We studied 300 women with abnormal uterine bleeding examined at the Clinic of Obstetrics and Gynecology at Saint Marina University Hospital– Pleven. Specimens for endometrial cytology were taken from all patients before invasive intervention. We compared the cytological results to evaluate the test validity, including sensitivity, specificity, and negative and positive predictive value in the cases with endometrial carcinoma. Statistical data processing was performed using the software programs MS Office Excel 2019 and IBM SPSS Statistics 28.0. The significance of results, findings and conclusions was determined at $p < 0.05$. A comparative analysis was performed on the cytological and histological results we obtained before and after the invasive manipulation. The study found statistical significance between the Pipelle biopsy results and cytological results ($\chi 2 = 50.05$, $df = 24$, $p = 0.01$, Cramer's $v = 0.439$). Data analysis showed that endometrial cytology had a high specificity in proving endometrial carcinoma and a low positive predictive value (Se = 80%; Sp = 98%; PV = 66.7%; NV = 96.9%). Endometrial cytology could be an effective diagnostic method and can be applied to diagnose endometrial pathology. The combination of the two methods - cytological examination and transvaginal ultrasound would undoubtedly improve the detection rate of endometrial carcinoma. Additionally, cytology is an appropriate outpatient procedure that can be recommended for endometrial screening, especially in patients at high risk of developing endometrial cancer.

**Key words:** Abnormal uterine bleeding (AUB), endometrial cytology, histological examination



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## Introduction

Endometrial carcinoma is the most common malignant tumour of gynaecological origin in developed countries. Its frequency is increasing worldwide and it is expected to rise further due to population ageing and the incidence of obesity in all age groups (World Cancer Research Fund International 2024). Endometrial carcinoma presents at an early stage with postmenopausal bleeding. Only in about 15% of cases is such a diagnosis given to premenopausal patients.

Endometrial carcinoma screening guidelines are only advisory. The lack of high-quality programs for primary prevention, low health awareness, the constantly decreasing number of health workers, poorly organised submission, collection and archiving of data, lack of an effectively implemented multidisciplinary approach, as well as the detection of oncological diseases in late stages, all require considerable financial resources and continuous funding of the health care system (Danon et al. 2003).

Braun et al. (2016) concluded that the best approach to diagnosing endometrial carcinoma combines transvaginal ultrasonography and endometrial biopsy. The authors emphasise transvaginal ultrasonography as the first choice of examination. The explanation for this emphasis is that the method is readily available, highly sensitive and cost-effective.

Olatunde et al. (2024) reported that the final diagnosis is based on the histological result from endometrial biopsy. Other readily available diagnostic tools include hysteroscopy and MRI for assessing endometrial thickness and/or structural abnormalities in the uterus. These modern imaging techniques and trained personnel have greatly improved and helped diagnose endometrial carcinoma, especially in developing countries.

Attempts to establish a screening program for endometrial cancer started over 30 years ago. Performing routine screening is economically unfeasible due to inappropriate diagnostic procedures that do not meet the screening criteria. Routine screening can be applied effectively in risk groups of women. A sufficiently reliable screening program has not yet been found because the PAP test is positive only in half of the cases, making it unsuitable for mass screening.

Active monitoring of risk groups is necessary for the early detection of endometrial carcinoma (EC). The initial recommendations are to cover women at increased risk, e.g., with HNPCC mutations, endometrial precarcinomas, or taking antiestrogen therapy for breast carcinoma. In such cases, endometrial cytology and/or biopsy are recommended from age 35 (Tropé and Makar 1991). As a counterpoint to the need for mass screening for endometrial cancer, Robertson (2003) stated that because most cases of endometrial cancer are diagnosed at an early stage, there is no evidence that mass screening with currently available technologies would be beneficial. The same study found that detection of endometrial carcinoma in asymptomatic patients did not improve prognosis.

The application of the PAP test of the cervix is based on the possibility of endometrial cells getting into the cervical canal, which directs us towards performing additional tests. One of the cheapest, safest and most reliable methods is endometrial cytology. There are studies in which different devices are applied to take cytological material from the uterine cavity in outpatient settings, as well as comparative studies and comparisons of their effectiveness (Kobayashi et al. 2010; Norimatsu et al. 2020).

Instruments with negative pressure are used to obtain material for the study of endometrial cytology. The most commonly used ones are Li brush, Tao brush, Endoram (SAP-1), and Uterobrush, among others (Munakata 2022).

The test validation criteria of sensitivity, specificity, and positive and negative predictive values are important because a false negative test result may delay seeking medical attention even if symptoms are present. False positives can lead to more tests, usually more invasive, such as dilatation and curettage, and hysteroscopy in a hospital setting under general anaesthesia, with more risks for the patient. The advantage in outpatient settings is the avoidance of general anaesthesia (patients with severe general diseases, polyallergies), the possibility of repeated sampling, and work capacity loss.

This study aims to determine the validation of the criteria: sensitivity, specificity, negative and positive predictive value in endometrial cytology compared with the histological result from the examined tissue samples.

## Material and methods

A prospective study included 300 women who visited the Clinic of Obstetrics and Gynecology at Saint Marina University Hospital– Pleven.

Criteria for inclusion in the study:

- age over 18 years;
- abnormal uterine bleeding;
- hospitalisation for invasive manipulation.

In all patients, material for cytological examination was taken from the cervical canal using a Cerviram and from the endometrium through an Endoram cannula. An endometrial biopsy was performed with a Pipelle aspiration cannula before invasive intervention. A comparative analysis was made after obtaining the laboratory results of the specimens collected before and after the invasive intervention. The sensitivity, specificity, and negative and positive predictive value of endometrial cytology in endometrial carcinoma were evaluated.

Statistical data processing was performed using the software programs MS Office Excel 2019 and IBM SPSS Statistics 28.0. The significance of results, findings and conclusions was determined at $p < 0.05$.

The following criteria were applied to assess the validity of the diagnostic method:

- Test sensitivity (Se) is the proportion of true positive subjects for the given disease. This criterion assesses the ability of the diagnostic or screening test used to detect individuals with a disease. We used the following formula to calculate the sensitivity: $Se = a/(a + c)$.
- Specificity (Sp) characterises the ability of the test to obtain normal or negative results for a person who does not have the disease or is the percentage of subjects who are healthy. It is calculated by the formula $Sp = d/(b + d)$.
- A positive predictive value (PV) measures the probability of the presence of the disease in individuals with a positive test. The following formula was used to obtain the results: $PV = a/(a + b)$ (Parikh et al. 2008).

- A negative predictive value (NV) indicates the probability of the absence of disease in individuals with a negative test (Shreffler and Huecker 2023). The formula used for calculating the indicator was NV = $d$ /($c$ + $d$)

**Table 1.** Possible results of the diagnostic method.

| Results of the diagnostic method | With disease | Without disease | Total |
|---|---|---|---|
| Positive | *a*<br>True positive | *b*<br>False positive | *a* + *b* |
| Negative | *c*<br>False-negative | *d*<br>True negative | *c* + *d* |
| Total | *a* + *c* | *b* + *d* | |

## Results

The study included 300 female patients divided into four age groups. The percentage distribution of the participants, according to their age group, is as follows:

- up to 40 y. – 24.7% (74 patients)
- 40–50 y. – 28.0% (84 patients)
- 50–60 y. – 24.7% (74 patients)
- over 60 y.– 22.7% (68 patients)

The share of women in the age group 40–50 y. is the largest (Fig. 1).

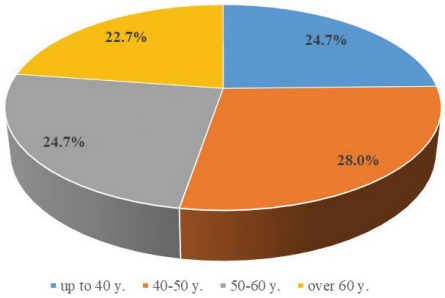


**Figure 1.** Distribution by age groups.

The data shows that the histological diagnosis from aspiration biopsy and the histological result from the surgical intervention/manipulation match in 81.3% of cases (244 patients). Differences in histological diagnoses were found in 18.7% (56 patients) (Fig. 2).

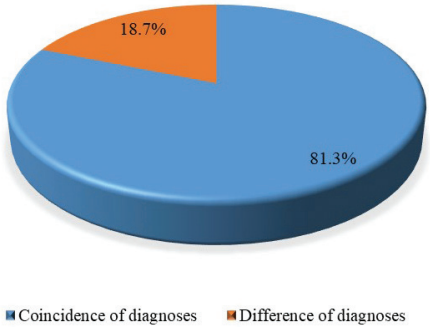


**Figure 2.** Concidence and difference of final diagnoses.

We compared the results obtained through histological and cytological investigation of biopsy samples collected using aspiration biopsy.

Of the 244 patients, in 83.6% the results from cytology investigations placing them in Group 2. (Fig. 3).

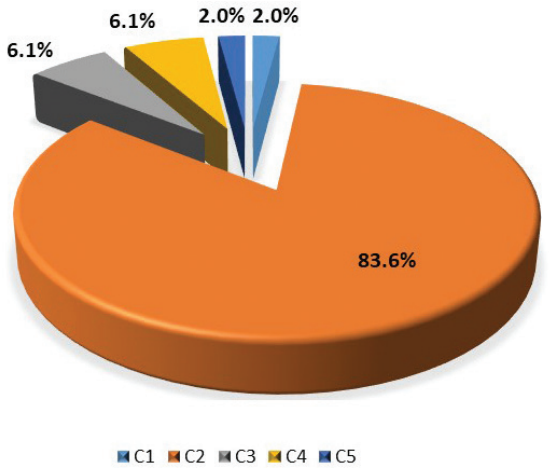


**Figure 3.** Percentage of matching diagnoses distribution.

The results were interpreted according to the International Cytology Reporting System, which is composed of 5 groups (Pinto et al. 2020):

- 1st group: non-diagnostic result (C1)
- 2nd group: negative for malignancy (C2)
- 3rd group: presence of atypia of undetermined significance (C3)
- 4th group: results suspicious for malignancy (C4)
- 5th group: positive for malignancyt (C5).

A comparative analysis was performed between the obtained cytological and histological results before and after the invasive manipulation. The study found statistical significance between Pipelle biopsy result and cytological result ($\chi 2 = 50.05$, df = 24, $p = 0.01$, Cramer`s v = 0.439), but no such relationship was present between the permanent histological result of the invasive intervention and the cytological result ($p > 0.05$).

The test's sensitivity, specificity, positive and negative predictive values in endometrial carcinoma were calculated to determine the diagnostic value of endometrial cytology. The results obtained were as follows:

In cases of endometrial carcinoma:

**Sensitivity –** the ability of the test to detect individuals with disease. It was calculated according to the formula $Se = a / (a + c)$, with the letters replaced by values corresponding to the characteristics in Table 1. The result shows that the Se of endometrial cytology is 80% for detecting endometrial carcinoma.

**Specificity –** the ability of the test to detect healthy individuals. It was calculated as the ratio of true negative cases to false positive cases + true negative cases. It is calculated by the formula $Sp = d /(b + d)$. Sp of endometrial cytology was 98% specific for proving carcinoma.

Positive predictive value is the probability of having a disease in individuals with a positive test. Our study proved that, in endometrial carcinoma, this indicator was 66.7%. Calculations were made according to the standard formula for positive predictive value (PV = $a$ /($a$ + $b$)).

Negative predictive value is the probability of absence of disease in individuals with a negative test. It was calculated as the ratio between the number of true positives and the number of true positive cases + false positive cases, using the formula NV = $d$ / ($c$ + $d$). The results showed that endometrial cytology has a 96.6% negative predictive value for diagnosing endometrial carcinoma.

## Discussion

Wang et al. (2023) conducted a systematic review and meta-analysis of the diagnostic accuracy of endometrial cytology in diagnosing endometrial cancer. The authors reported differences in the test's sensitivity when sampling with different instruments. Their data proved that the Se of the results for materials taken with the SAP-1 cytology collector was 84%. The Endoram cannula, which is part of the SAP-1 group, was mainly used in our study. Comparing the data analysed by Wang et al. (2023) with our test sensitivity results (Se = 80%) also supports the proposition that endometrial cytology has a high sensitivity rate for detecting endometrial carcinoma.

Wang et al. (2019) conducted a meta-analysis of endometrial cytology as a diagnostic method for endometrial carcinoma. The analysis proved the high diagnostic accuracy of the procedure and a test sensitivity of over 90%. Our data showed a smaller percentage of Se (80%). Nevertheless, it can be concluded that endometrial cytology has a high diagnostic value in proving endometrial cancer.

By conducting a study among 917 women, Buccoliero et al. (2007) proved that endometrial cytology for the diagnosis of endometrial carcinoma has a negative predictive value of 99%. The findings from our study are close to these results (Np = 96.6%), which proves that this diagnostic method can be used effectively in diagnosing endometrial cancer. Nakagawa-Okamura et al. (2002) also reported using endometrial cytology as screening for endometrial carcinoma. Therefore, organising early screening would lead to early screening would lead to early diagnosis of the disease and even improve survival in those diagnosed (Nakagawa-Okamura et al. 2002).

## Conclusion

Endometrial cytology is an effective diagnostic method for endometrial carcinoma. The combination of the two methods – cytological examination and vaginal ultrasound will definitely improve detection of endometrial carcinoma. Cytology is an appropriate outpatient procedure that can be recommended for endometrial screening, especially in patients at high risk of endometrial cancer.

## Additional information

### Conflict of interest

The authors have declared that no competing interests exist.

## Ethical statements

The authors declared that no clinical trials were used in the present study.

The authors declared that no experiments on humans or human tissues were performed for the present study.

Informed consent from the humans, donors or donors' representatives: University Hospital Saint Marina – Pleven.

The authors declared that no experiments on animals were performed for the present study.

The authors declared that no commercially available immortalised human and animal cell lines were used in the present study.

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## Author contributions

Conceptualization: KT, TT. Data curation: TKS. Formal analysis: EP, TKS, TT. Investigation: MN, DGD. Methodology: NH. Project administration: KT, EP, NH. Resources: MN, TT. Software: EP, DGD. Supervision: NH. Validation: MN, KT, DGD, TKS. Visualization: TKS, DGD. Writing – original draft: EP. Writing - review and editing: NH.

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## Data availability

All of the data that support the findings of this study are available in the main text.

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