A THIN AND REGULAR ENDOMETRIUM IN ENDOMETRIAL CANCER - ENDOVAGINAL ULTRASOUND ASSESSMENT

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A THIN AND REGULAR ENDOMETRIUM IN ENDOMETRIAL CANCER- ENDOVAGINAL ULTRASOUND ASSESSMENT (Abstract): Aim: Our study had as a major objective the highlighting of more objective criteria in establishing the morphological diagnosis and the evaluation of prognosis elements in endometrial hyperplasia and endometrial carcinoma, representing a specific pathology for the premenopausal and postmenopausal women. Endometrial adenocarcinoma is a malignant tumor, rare in women under 40 years of age, but the incidence increases after menopause, gradually reaching a maximum between 70-79 years.

Material and methods: The study included 291 patients with endometrial adenocarcinoma. The patients were admitted in 2005-2010 to “Cuza-Voda” Obstetrics and Gynecology Hospital in Iasi. The study group was diagnosed and investigated on the basis of the clinical examination and the specialized complementary explorations. The histopathological diagnosis was obtained by the processing of the hysterectomy specimen. Results: The results of the study that we conducted highlight the fact that nearly half of the patients diagnosed with endometrial adenocarcinoma were 50-59 years old. In 78.01% cases the uterus was of normal size, between 4-6cm, in 10.31% cases was increased over 6 cm and 11.68% it was of small size, less than 4 cm.

Conclusions: The study recommends surveillance of cases with endometrial hyperplasia especially if are associated with incriminated risk factors in the etiology of carcinoma of the uterus.

Keywords: ADENOCARCINOMA, ENDOMETRIUM, ULTRASONOGRAPHY.

In the current gynecological practice there are many uterine lesions, many of which may be associated with abnormal uterine bleeding, and for this reason they should be excluded before diagnosing a dysfunctional uterine bleeding. In pre- and postmenopausal women, the most frequent morphological substrate of abnormal uterine bleeding is the hyperplasia of the endometrium and the endometrial carcinoma (1). The noninvasive diagnosis of such bleeding can be done through endometrial cytology, endovaginal ultrasound and tumor markers (2).

The endometrial cytology has limited value because it is an indirect method, the results of which are encumbered on the one hand by false-negative results due to the
fact that the malignant endometrial cells rarely exfoliate spontaneously and if such phenomenon occurs, they undergo a number of changes during the passage through the genital tract. If endometrial cytology is sampled directly with a brush or by washing, the results are more precise (3).

The tumor marker is not specific to the endometrial carcinoma - CA 125 and, in the early phase of the disease, it is not increased so it did not constitute a diagnostic indication (4).

The endovaginal ultrasound (EEV) is currently accessible, non-invasive and painless and it is used frequently in the screening, assessment and monitoring of metrorrhagia in pre- and postmenopausal women (5).

Endometrial adenocarcinoma is a malignant tumor, rare in the Caucasian women under 40 years of age, but the incidence increases after menopause, gradually reaching a maximum between 70-79 years. The women of the black race, the maximum incidence of the endometrial adenocarcinoma is reported in premenopausal, with a rate of 85 cases per 100,000 women annually.

EH is considered to have increased risk of endometrial carcinoma. It is a common condition and it includes a wide spectrum of histological changes, from the simple aggregation of glandular proliferation with normal appearance, to changes difficult to distinguish from endometrial carcinoma. The EH diagnosis raises three issues: the first relates to the reproducibility of less than 50% between observers; the second is the finding that around 50% of the cases with atypical hyperplasia (AH) have also carcinoma lesions, and the third stems from the fact that the data about the progressive risk of evolution of EH towards the endometrial carcinoma are limited. Current data shows that, in the long term, the risk of developing endometrial carcinoma is less than 5% for women with simple hyperplasia (SH) or complex hyperplasia (CH) but it is of up to 30% for those with atypical hyperplasia (AH).

MATERIAL AND METHODS

Endometrial adenocarcinoma is a malignant tumor, rare in women under 40 years of age, but the incidence increases after menopause, gradually reaching a maximum between 70-79 years.

The study included 291 patients with endometrial adenocarcinoma. The patients were admitted in 2005-2010 to "Cuza-Voda" Obstetrics and Gynecology Hospital in Iasi. The study group was diagnosed and investigated on the basis of the clinical examination and the specialized complementary explorations. The histopathological diagnosis was obtained by the processing of the hysterectomy specimen. We used the data recorded in the observation charts and the computerized system.

The data collected as a study material and considered refer to: the total number of cases of endometrial carcinoma, diagnosed and operated, the annual distribution of the cases, the repartition of cases according the age groups, the type of the invasion of the tumor tissue myometrium, distribution of cases according to the length of the uterine cavity.

Even though the number of cases hospitalized and operated on different gynecological diseases was on the rise at our hospital between 2005-2010, this was not seen in the case of endometrial adenocarcinoma. The maximum number of cases was, at the beginning of the study, years 2005-2007 (96 cases), 2.87% of the surgeries during that period.

In the studied cases, the results of the endovaginal ultrasound exam are relevant.
For the 291 patients with endometrial carcinoma, the local vaginal exam combined with the abdominal palpation and correlated with the endovaginal ultrasound established the size and thickness of the endometrium of the uterus.

Our study, consisting of the two groups of endometrial adenocarcinoma, shows that between the endometrioid and the non-endometrioid adenocarcinoma there are significant differences regarding the invasion in the myometrium.

**RESULTS**

Of the total number of patients included in the study, 25% are between 33 and 53 years old, and 50% are up to 58 years old. Most cases of endometrial adenocarcinoma, in our study, have been reported in patients aged 53 (modal or dominant value).

The results of the study that we conducted highlight the fact that nearly half of the patients diagnosed with endometrial adenocarcinoma were 50-59 years old. Among the 291 patients, 268 (92.1% of the total) were postmenopausal.

In the study that we conducted, the diagnosis of admission was neoplasm of uterine body in 197 (67.7%), endometrial polyp in 6 (2.06%), uterine fibroid in 59 (20.27%) and hemorrhages in peri climax in 29 (9.97%).

Another important factor of the prognosis for the patients with endometrial adenocarcinoma refers to the invasion of the tumor tissue myometrium.

Among the 291 studied cases, in 9 patients (3.09%) the tumor tissue has not infiltrated the myometrium; in 148 (50.85%) the myometrium has been infiltrated in a proportion of not less than 50% (the infiltration was limited to the internal half of the myometrium), while in 134 (46.06%) the myometrium showed a tumor infiltration of more than 50% cases.

The results obtained in our study reveal that over half of the cases showed evidence of the presence of lymphatic invasion in the vessel-lymphatic area (157; 53.95% of the studied cases). By age groups, the invasion of the vessel-lymphatic area was at its maximum for the patients falling in the range of 50-54 years (43; 14.78% of the patients included in the study).

Depending on the distribution of the endometrial adenocarcinoma according to the length of the uterine cavity in over 60% of the cases, the uterine cavity size was over 4 cm, and in a quarter of cases studied by us it was of 4 cm. Uterine cavity has a normal length of between 3-5 cm. In the cases included in the study, the uterine cavity length, assessed according to the hysterectomy specimen, was in average 5.019 ± 1.494 cm. Most often we found a value of 4 cm of length of the uterine cavity, but the limits of variation for the studied cases were very high. Therefore, the smallest length recorded was 2 cm, and the maximum recorded value was of 14 cm.

In our study, from the 291 cases of endometrial adenocarcinoma, in 205 (70.44%) by way of ultrasound it was reported the coexistence of hypertrophic or atrophic changes of the endometrium. Adenocarcinoma cases were included in two groups, the first group having 43 patients (20.98%) with endometrial adenocarcinomas associated with hypertrophy that histologically have proven to be hyperplasia and the second group represented by 162 (79.02%) with adenocarcinoma developed onto an atrophic endometrium.

In 86 (29.55%) cases there was not any ultrasound identification of hypertrophic or atrophic aspects of the endometrium.

The histopathological diagnosis was specified on histological sections taken.
from the pieces of the surgical resection. In all cases the histological grading was established, along with the invasion of the myometrium.

The value of the endovaginal ultrasound in the diagnosis of the endometrial carcinomas is relevant. Depending on the size, the size of the uterus was divided into three categories: normal size, reduced size and increased volume. The size of the uterus was established following a clinical exam correlated to the endovaginal ultrasound. (fig. 1).

In 227 (78.01%) of the cases the uterus was of normal size, between 4-6 cm; in 30 (10.31%) cases its volume was increased, over 6 cm, and in 34 (11.68%) cases it was of small size, less than 4 cm.

![Fig. 1. Distribution of cases depending on the size of the uterus](image)

The total thickness of the endometrium has been measured in the sagittal plan, endovaginal, including any area of focal thickening. The presence of areas with high echogenity, which interrupted the normal trilaminar structure of the endometrium pointed out to an endometrial pathology (fig. 2).

![Fig. 2. Endometrium thickness determined by endovaginal ultrasound](image)

In 275 (94.50 %) patients with endometrial carcinoma from our study, the endometrium thickness determined by endovaginal ultrasound was averaging 15 mm, with limits between 5 and 65 mm. In 16 (5.5%) patients with endometrial carcinoma, the
endometrium thickness determined by endovaginal ultrasound was under 5 mm, with limits between 5 and 4.5 mm (fig. 3).

In the case of patients with endometrium thickness under 5 mm, studying the observation sheets, the anamnesis (clinical history and menstrual status) revealed that in the last 3 months, prior to admission, these patients have undergone uterine cavity curettage, that all the patients were between 60 and 69 years old, they were in postmenopausal, and the histopathological examination has identified different types of endometrial carcinoma.

**DISCUSSION**

From the clinical and ultrasound study of 291 endometrial adenocarcinomas, there are a few issues that need to be highlighted and discussed in the light of the recent data from the medical literature.

Our study proves that endometrial hyperplasia are a common diagnosis in pre- and postmenopausal patients, they are often identified as a result of investigations for abnormal uterine bleeding; these are issues that should be considered by the gynecologist during the routine consultations and it is subsequently required an endovaginal ultrasound for the assessment of the thickness of the endometrium.

Most authors (6) consider that measuring the thickness of the endometrium through the EEV is a method with high specificity for the diagnosis of the endometrial carcinoma, especially in postmenopausal women. According to the results in the literature (7), the normal limit thickness of endometrium in postmenopausal women is 5 mm, and above it the endometrium biopsy with histopathological interpretation is required, but some results concerning the linking of the over 5 mm thickness of the endometrium to EEV with severe endometrial pathology would be of only 4% (8). Studies on the histology of a 6 mm thick endometrium at EEV showed a specificity of 98%, but a sensitivity of only 17% which leads to the conclusion that EEV is not an appropriate method for the screening of the endometrial carcinoma (9). Another study published results showing that using for EEV a limit value of 4 mm thickness of endometrium in women with postmenopausal bleeding both for those who used hormonal substitute treatment (estrogen and progesterone) and those without such treatment, the sensitivity in detecting the endometrial carcinoma was 100% and the specificity of 60% (10).

Normal endometrium has a thickness of under 5 mm in postmenopausal women and its borders must be regular and visible throughout the uterine cavity. For the interpretation of the thickness of the endometri-
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In our statistics (10) we took into account the literature data, which show that the endometrium with a thickness greater than 5 mm in postmenopausal women is associated with an increased probability of the existence of a hyperplasia or an endometrial carcinoma, and any focal lesion of the endometrium, revealed at endovaginal ultrasound, regardless of the thickness of the endometrium, requires endometrial biopsy.

Our results confirm the data from the literature (11), showing that the endometrial adenocarcinoma in postmenopausal patients can be associated with a thin endometrium, with a thickness under 5 mm.

However, such cases published in the literature are rare. Thus, until 2007, founds in the literature only 14 authors who reported cases of endometrial adenocarcinoma in postmenopausal patients, where the endovaginal ultrasound showed a thickness of under 5 mm of the endometrium (12,13).

With the help of the endovaginal ultrasound with pulsed Doppler it is identified, highly accurately, the presence of the endometrial adenocarcinoma, which determines the decrease of the number of false-positive results (14).

The studies published in the literature specify that tumor infiltration in the myometrium is associated with a poor prognosis. Adenocarcinomas limited only to the endometrial mucosa have a survival rate of over 95% at 5 years (15).

CONCLUSIONS

Our study revealed that the endovaginal ultrasound assessment of the thickness of endometrium, is absolutely necessary in the diagnosis of the endometrial lesions and it has an important role in the screening of endometrial adenocarcinoma. The endovaginal ultrasound can provide orientation in more than 90% of the cases, the existence of a proliferative lesion of the endometrium in postmenopausal women, where the thickness of the endometrium is greater than 5 mm.

Also, our study had as a major objective the highlighting of more objective criteria in establishing the morphological diagnosis and the evaluation of prognosis elements in endometrial hyperplasia and endometrial carcinoma, representing a specific pathology for the premenopausal and postmenopausal women.

If the endovaginal ultrasound reveals the endometrium with a thickness of less than 5 mm and regular layout, in patients that are in pre- and postmenopausal at increased risk and abnormal uterine bleeding, who underwent a previous biopsy, within a period of less than three months from the date of the first submission, the uterine curettage is necessary for a more accurate histological diagnosis.

REFERENCES


**NEWS**

PERFORMANCE OF MOLECULAR TESTS IN THE DETECTION OF TRICHO PHYTON SPECIES

Dermatophytosis caused by *Trichophyton* and *Microsporum* species represent the most frequent mycoses worldwide. Molecular detection methods are highly sensitive and allow for rapid and accurate identification of dermatophytes from clinical specimens. Kupsch et al investigated the sensitivity of different molecular methods compared with conventional diagnostics (culture) in the detection of dermatophytooses caused by *T. rubrum* and *T. interdigitale* in 375 clinical samples of nail, skin and hair. The compared molecular methods included already published PCR-ELISA assays, qRT-PCR as well as a newly developed PCR-ELISA targeting the internal transcribed spacer region. In 39.5 % of cases a positive result was obtained in at least one molecular test or by culture. The results showed that the most sensitive test was a PCR-ELISA targeting a microsatellite region which identified 81 *T. rubrum*-infections followed by an ITS PCR-ELISA (60), qRT-PCR (52) and a topoisomerase II PCR-ELISA assay (51); significantly, cultivation detected *T. rubrum* in only 37 samples (Kupsch C, Ohst T, Pankewitz F, Nenoff P, UhrLaß S, Winter I, et al. The agony of choice in dermatophyte diagnostics - Performance of different molecular tests and culture in the detection of *T. rubrum* and *T. interdigitale*. Clin Microbiol Infect. 2016 May 30. pii: S1198-743X(16)30142-2. doi: 10.1016/j.cmi.2016.05.015).