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## CLINICO-MORPHOLOGICAL CHARACTERISTICS OF PATHOLOGICAL PROCESSES IN THE ENDOMETRIUM OF PATIENTS AT THE PREMENOPAUSAL AND POSTMENOPAUSAL PERIODS

**Abstract:** *Despite the undeniable successes of modern medicine, the urgent problems of oncology and, in particular, oncogynecology are still unresolved. In our study, 132 patients were referred to the Oncology clinic of AMU, having proliferative changes in the endometrium, including those with cancer of the body of the uterus. Considering that complaints in patients with uterine cancer appear before the menopausal period, the most important and key factor for successful detection and treatment is the correct diagnosis and timely correct approach to patients with proliferative and malignant changes in the body of the uterus. Compliance with the correct algorithm, the amount of research, and the correct implementation of the surgical manual can significantly improve the results of treatment. The article will discuss the proliferative changes and their transformation to endometrial cancer in the pre- and postmenopausal periods.*

**Key words:** pre- and post-menopausal periods, uterine cancer, malignant processes, proliferation.

**Language:** English

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### Introduction

One of the main tasks of modern oncology is to study various aspects of the pathogenesis of benign and malignant proliferative processes in the endometrium. Hyperplastic processes of the endometrium are sometimes considered as one of the first signs of neoplastic cell transformation and the development of adenocarcinomas. The incidence of transition from endometrium atypical hyperplasia to cancer varies from 23% to 57% [8, p. 91-96]. Malignant transformation of proliferative processes during 1-14 years was 2-5% in the background of

glandular cystic hyperplasia, 15% in metaplasia of squamous cells, and 30-32% in the background of adenomatous hyperplasia [9, p. 2607-2618].

In modern times, there is a steady increase in morbidity and mortality due to neoplasms of the female reproductive system. This trend depends on many factors, including hormonal changes in the organism, genetic factors, precancerous conditions, and their development, as well as the timely detection and treatment of the disease. An increasing trend in the demographic indicators of the world's population has been observed in recent years. Thus, according to

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statistics, in 2010 the world's older generation was 750 million. It can be assumed that in 2020 it will reach 1 billion. Based on the above data, in 2050, people in the age group of 65 years old and older will make up 16% of the world's population. An interesting point is that the majority of people in this group are women [4, p. 250]. Thus, we should emphasize the importance of age and age-related physiological processes in the female organism and most importantly, the pathological changes in the hormonal background.

From an oncological point of view, the age factor is one of the main risk factors involved in the formation of new malignant tumors [6, p.237–259; 7, p. 107474]. Thus, an increase or decrease in the hormonal balance of the female reproductive system, especially the ovaries, is characterized as premenopausal and postmenopausal periods in the female body. Due to age, cells accumulate in various organs and tissues in the body, which in turn stimulates the development of malignant processes in the future, and under the influence of various carcinogenic factors, the cells become malignant. It is believed that the effect of carcinogenic factors is directly proportional to age [1, p. 256].

According to recent reports, the incidence of malignant diseases of the female reproductive system reaches its peak in people aged 55-65 years. However, modern data, including our personal research, indicate the early onset of premenopausal and postmenopausal periods due to nutritional factors, lifestyle changes, the rise of civilization, etc. [2, p. 6–12; 3, p.185–8].

An examination of 396 patients with uterine body cancer in the United States between 2014 and 2016 showed a more aggressive and unfavorable course of the disease in the postmenopausal period. The incidence of carcinomas was determined in two groups of women: premenopausal (45-55 years old) and postmenopausal women (60 years old and older) groups. Morphologically, the incidence of carcinomas was higher in the II group women compared to the I group [5, p. 44-47]. Another study revealed that in patients between the ages of 70 and 75, serous and poorly differential forms of endometrial cancer (EC) occurred more than in women aged 45-55 years.

Proliferative changes in the endometrium (hyperplasia, atypical endometrial hyperplasia, endometrial cancer) are known to be manifested by atrophic processes in the endometrium, the inner lining layer of the uterus, destruction, and degradation of glandular tissue, in short, the destruction of the

cellular nuclear complex. These changes result in the formation of poorly differentiated, endometrial intraepithelial neoplasms and cancer cells.

### The purpose of the study.

Clinical characterization of proliferative and malignant processes in the endometrium of women at the premenopausal and postmenopausal periods, and the application of our results in medical practice.

### Materials and methods.

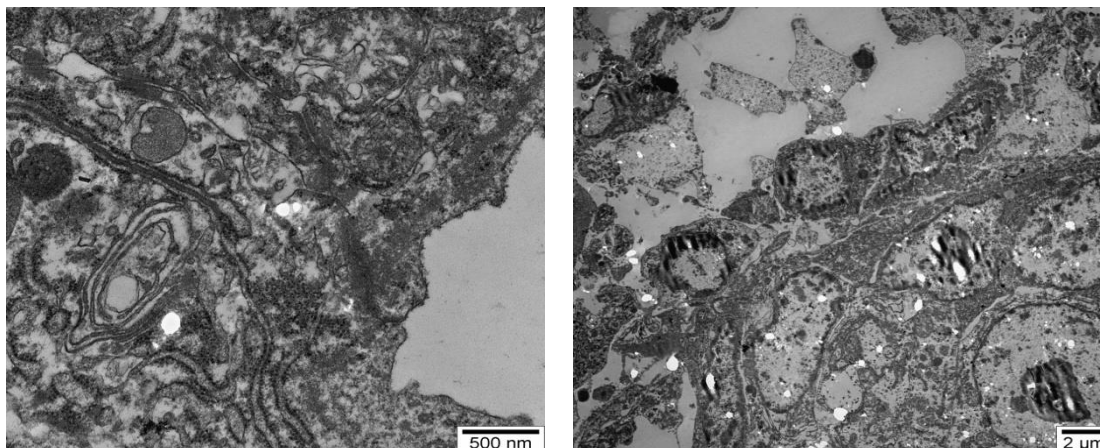
Our study was conducted on 167 patients in the premenopausal and postmenopausal periods who were referred to the polyclinic and oncogynecology department of the Oncology Clinic of AMU in 2016-2018 for examination and treatment. Our study included patients who applied to our clinic for examination and treatment, were registered in the clinic, and based on ultrasound examination, had a history of endometrial thickening, i.e. hyperplasia. Based on anamnestic data and complaints (concomitant diseases), these patients underwent physical, clinical, laboratory, instrumental examinations, MRI and, if necessary, contrast CT examination, as well as a smear test.

In this group of patients special attention was paid to the laboratory tests such as general, biochemical examination of blood, coagulogram, and especially to the indicators of oncomarkers (CA-125, 15.3, sometimes CEA). Based on the results of the performed examinations, as well as the pathomorphological study of smear materials, methods of treatment were chosen for the patients in the premenopausal and postmenopausal periods.

In clinical practice, the smear test of the mucous membrane of the uterus and its pathohistological examination is the leading diagnostic method in the study of proliferative processes of the endometrium [10, p. 2129-2136]. However, in 18-29% of cases, endometrial cancer (EC), detected after a total hysterectomy, may not be found by the preoperative smear test used to diagnose invasive cancer in these patients. In 38-42% of the cases, the results of the pre- and postoperative tests coincided [11, p. 804-811]. In our study, pathomorphological examinations of pre- and post-endometrial diagnostic smear preparations were conducted. In some groups of patients, both pathomorphological and electron microscopic examinations of surgical materials were performed.

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**Figure 1a. Poorly differentiated endometrial adenocarcinoma.**  
**1b. Most of the cells are lysed.**

**Results and Discussion.**

In our study, endovaginal ultrasonography revealed endometrial thickening in 31 (82.6%) patients with atypical glandular hyperplasia (AVH) and in 109 (88.6%) patients with endometrial cancer (EC). In some cases, sonography can be used to obtain information about the invasion of the tumor into the myometrium. Ultrasound examination revealed not only the thickness and structure of the inner layer of the uterus but also using the Doppler mode allowed us to determine the characteristics of vascularization. The heavy bleeding of the pathological focus allowed us to speculate as to whether the process was malignant. In our study, neovascularization of the changed areas was identified in 53.8% (71 cases) of endometrial carcinoma cases. In atypical glandular hyperplasia cases, this parameter was 22.8% (8 cases) ( $p < 0.05$ ). It should be noted that the foci of neovascularization were more pronounced in the

middle M-echo projection. In cancer, vascularization was presented by several nourishing vessels and was chaotic. Of the 132 patients diagnosed with cancer, 35 (26.5%) had a tumor in the upper part of the uterine body, 27 (20.4%) in the lower 1/3 of the uterine body, and 31 (23.5%) in the central part of the uterus; In 18 (13.6%) patients, the uterine cavity was completely filled and in 21 (15.9%) patients, cervical damage was detected. In addition to the US examination, 87 patients with uterine body cancer were examined by MRI, 74 of whom were diagnosed with myometrial invasion, and 13 patients with cervical invasion. According to the MRI examination, the rate of metastatic damage to regional lymph nodes was 9 (10.3%). This method allowed us to assess the degree of invasion of the tumor, the condition of the regional lymph nodes, the clinical stage of the disease, as well as to choose appropriate surgery. The results obtained are described in Table 1.

**Table 1. Stage distribution of patients with endometrial cancer**

Age of the patients	Stage of the disease						Total
	IA	IB	II	IIIA	IIIB	IIIC	
<39	7 (87.5%)	1 (12.5%)	-	-	-	-	8
40-49	11 (78.6%)	2 (14.3%)	1 (7.1%)	-	-	-	14
50-59	40 (71.4%)	9 (16.1%)	3 (5.3%)	2 (3.6%)	-	2 (3.6%)	56
60-69	20 (51.3%)	11 (28.2%)	4 (10.2%)	3 (7.7%)	-	1 (2.6%)	39
>70	7 (46.6%)	5 (33.3%)	1 (6.7%)	1 (6.7%)	-	1 (6.7%)	15
Total	85 (64.4%)	28 (21.2%)	9 (6.8%)	6 (4.6%)	-	4 (3.0%)	132

In the patients, we examined and treated, the vast majority of malignant processes of the endometrium occurred in stage I. As seen in the table, endometrial cancer was more common in stage IA during the reproductive, climacteric, and menopausal

periods. Stages IA and IB in the <39 age group were observed in 7 (87.5%) and 1 (12.5%) cases, respectively, in the 40-49 age group in 11 (78.6%) and 2 (14.3%) cases, in the 50-59 age group in 40 (71.4%) and 9 (16.1%), in the 60-69 age group in 20

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(51.3%) and 11 (28.2%) cases, in the >70 age group in 7 (46.6%) and 5 (33.3%) cases.

According to our results, stage IA occurred in 85 (64.4%), stage IB in 28 (21.2%), stage II in 9 (6.8%), stage IIIA in 6 (4.6%), and stage IIIC in 4 (3.0%) cases.

In our study, well, moderately, and poorly differentiated types of endometrioid adenocarcinomas were observed. The distribution of different histological variants depending on age and pathomorphological structure is described in Table 2.

**Table 2. Distribution of patients depending on their age and pathomorphological structure of the tumor**

Results of the histological examination	Age				P
	< 60 years old		> 50years old		
	Absolute value	%	Absolute value	%	
Endometrial AdCa G1	59	37.1	28	17.8	<0.05
Endometrial AdCa G2	76	47.8	78	49.68	>0.05
Endometrial AdCa G3	11	6.92	17	10.83	>0.05
Open cell carcinoma	3	1.88	6	3.8	>0.05
Serous carcinoma	7	4.4	25	15.9	<0.05
Mucinous ADCA	3	1.88	1	0.63	>0.05
Total	132	100	155	99	

**Conclusion.**

Thus, according to our research, a high rate of transition to malignant processes due to many diseases, especially proliferative changes in the endometrium, is characteristic of premenopausal and postmenopausal women. In this regard, educating patients, establishing the existence of the history of bloody discharge in the postmenopausal period, age and concomitant diseases, especially triad (hypertension, diabetes, obesity), including long-term hormonal therapy (tamoxifen intake, infertility, and treatment of polycystic ovaries) have a primary value for the early detection of the disease (early screening). In premenopausal and postmenopausal women, age and body mass index are directly proportional to the development of the disease.

Proliferative and malignant processes in the endometrium in the premenopausal and

postmenopausal periods are characterized not only by an increase in estrogen but also by impaired expression of steroid hormone receptors, with a high effect of biologically active substances on these indicators. In our study, 75% of patients with atypical hyperplasia and cancer had a history of adenomyosis, genital endometriosis, endometritis, including multiple mechanical effects on the endometrium (abortions, thermal coagulation), and patients with endometrial hyperplasia took a special place. In general, the results obtained will contribute to the prediction of the course of proliferative processes in our patients. This, in turn, will help reduce the spread of the disease and the number of patients who come to the clinic in the late stages of the disease and choose the right and appropriate treatment tactics.

**Reviewer:**

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