IMMUNOHISTOCHEMICAL CHARACTERISTICS OF ENDOMETRIAL TUMORS

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Abstract. Endometrial cancer in women over 50 years of age is more aggressive in terms of the histological type of tumor, the degree of its differentiation, and the stage of the disease, characterized by an unfavorable prognosis.
Keywords: morphology, endometrioid adenocarcinoma.

Relevance. Endometrial cancer (EC) is the sixth most common cancer in the world [1,3,5,7,9] and the third most common cancer in Uzbekistan [2] in the female population. Over the past 30 years, the incidence rate in Uzbekistan has increased by 132% [2,4,6,8] and is not expected to decline in the near future [1], reflecting the increasing prevalence of risk factors such as obesity and the continuing aging of the population [3,10,11,13]. According to United Nations projections, the proportion of people aged 65 and older in the global population will increase from 10% in 2022 to 16% in 2050 [1]. It is important to note that in most countries, including Uzbekistan, women constitute the majority of the elderly population [2, 12]. Given the emerging socio-demographic trend, an increase in the number of EC patients over 50 years of age is expected in the coming years. In 2020, the global incidence of newly diagnosed endometrial malignancies in the age group of 50 years and older was 25.6% (107,001 people). By 2040, this figure is expected to increase to 33.5%, representing approximately 204,000 people [3]. In Uzbekistan, in 2021, the same figure was 6,732 (26.4%) patients in the age group ≥ 50 years [15]. A review of the literature revealed that there are currently no uniform principles for the management of endometrial cancer patients over 50 years of age. This problem may be related to the underrepresentation of older patients, including those with endometrial cancer, in clinical trials on optimal treatment methods [12, 14]. Given that the 5-year survival rate for patients with localized forms of the pathological process reaches 74-92% [1, 14], it is expected that a significant number of elderly and senile patients treated for EC will be registered with oncology clinics. Therefore, proper monitoring and recommendations to reduce the risk of recurrence are essential. While a significant number of studies are currently underway to identify prognostic factors influencing the course and outcome of EC, these factors should be studied separately for older individuals, which was the reason for conducting this study.

Objective of the study. To determine the clinical and morphological features and prognosis of endometrial cancer in patients over 50 years of age.

Materials and methods. The study included 136 patients who were examined and treated from 2022 to 2025 in the gynecology department of an oncology hospital in the Kharezm region. Based on clinical, ultrasound, and other indications, the patients underwent surgical treatment (hysteroscopy with RDV) or hysterectomy) followed by morphological examination of the endometrial material. Inclusion criteria: 1. Patients who received primary surgical treatment in the gynecology oncology department; 2. Postmenopausal; 3. Histologically verified diagnosis of uterine cancer. Exclusion criteria: 1. Patients who received primary surgical treatment elsewhere; 2. Patients who received any special treatment before surgery; 3. History of cancer; 4. Histologically confirmed uterine sarcomas. Information on the incidence of DNA mismatch repair (MMR) defects and p53 protein status was available for 145 of the 259 cases included in the study: 97/48 patients in Group 1 and 128/131 patients in Group 2. All cases were divided into three subgroups based on molecular alterations: Group 1 – dMMR, n=88 (35.9%); Group 2 – p53abn, n=19 (7.8%); Group 3 – pMMR/p53wt, n=138 (56.3%). An initial analysis of the distribution of the main histological variants of EC depending on the spectrum of molecular alterations revealed that the pMMR/p53wt subgroup included 8 cases of serous carcinoma. Considering that 90% of serous endometrial tumors show abnormal (mutant type) p53 protein staining in IHC studies, which is a surrogate marker for the presence of a mutation in the TP53 gene [1,3], these cases were re-examined with subsequent IHC evaluation. In 5 of 8 cases, repeat immunohistochemistry revealed abnormal p53 protein staining, confirming the diagnosis of serous endometrial carcinoma. In 18 of 8 cases, wild-type p53 protein was detected, leading to a change in diagnosis to undifferentiated carcinoma G3 in 2 cases and endometrioid carcinoma G1 in 1 case. The obtained changes led to a minor adjustment of the previously published data [19] on the distribution of the main histological variants of EC in two age groups, which ultimately did not affect the conclusion that EC in patients ≥ 70 years old is characterized by a predominance of non-endometrioid neoplasms compared to patients in the 50-69 year old group, $p = 0.005$. In the dMMR and pMMR/p53wt subgroups, tumors were represented by the endometrioid histotype – 94.32% and 95.66%, respectively ($p = 0.645$) with a prevalence of low-grade carcinomas – 81.8% and 88.4%, respectively ($p = 0.166$), while in the p53abn subgroup, more than half of all cases – 68.5% – were non-endometrioid forms of the disease, with the main histological subtype being serous adenocarcinoma – 57.9%, $p < 0.001$.

An assessment of myometrial invasion by molecular subgroup revealed no significant differences between them, despite the fact that invasion of >1/2 of the myometrium was observed in most cases in the p53abn subgroup (p = 0.418), in contrast to tumor invasion into the cervical stroma, which was statistically more frequently observed in the p53abn subgroup – 36.8% versus 13.6% in the dMMR subgroup (p = 0.016) and 10.9% in the pMMR/p53wt subgroup (p = 0.002). It should be noted that the studied subgroups were comparable in terms of both the extent of surgical treatment and the adjuvant therapy administered in the postoperative period, which obviously excludes the possibility of influencing long-term results. The majority of all endometrioid carcinoma cases in the 50-69 year-old group fell within the pMMR/p53wt subgroup—72.8%, while non-endometrioid neoplasms fell primarily within the DNA mismatch repair deficiency subgroup—66.7%. The primary surgical treatment for patients included in the statistical analysis was extended panhysterectomy, performed in 174/245 (71%) cases, and the leading adjuvant therapy option in the postoperative period was radiation therapy, performed in 92.5% of cases (147/159). The specified volumes of specialized treatment in the 50-69 year-old group were predominant in the pMMR/p53wt subgroup – 70% and 72.5%, respectively; in the over-70 year-old group, in the subgroup with DNA mismatch repair deficiency – 52.4% and 48.7%, respectively, p < 0.001. For the remaining surgical treatment options and adjuvant therapy, no significant differences were found based on age or molecular subgroup. In both age groups, carcinomas from the subgroups with DNA mismatch repair deficiency and those without a specific molecular profile were characterized by similar prognoses, with no significant differences between them. In the 50-69 year old group, the 5-year overall, adjusted, and relapse-free survival rates of patients in the dMMR subgroup were 100%, 100%, and 71.4%, respectively, versus 95.6%, 97.8%, and 84.4%, respectively, in the pMMR/p53wt subgroup (p = 0.463, p = 0.603, and p = 0.275, respectively). In the group ≥ 70 years, the 5-year overall, adjusted, and relapse-free survival rates of patients in the dMMR subgroup were 79.2%, 90.5%, and 55.6%, respectively, versus 65.5%, 73.1%, and 51.8%, respectively, in the pMMR/p53wt subgroup (p = 0.273, p = 0.132, and p = 0.785, respectively).

Conclusions. Endometrial cancer in patients over 50 years of age is characterized by worse long-term results: 5-year overall, adjusted, and relapse-free survival rates were 69.4%, 78.1%, and 51.9% versus 96.2%, 97.4%, and 80.2% in the 50-69 year old group (p < 0.001).

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