

## **ANALYSIS OF ADVERSE PROGNOSTIC FACTORS IN ENDOMETRIAL CANCER**

Kuryozova Gulasal Komuljonovna

**Bukhara Medical Institute named after Abu Ali Ibn Sina.**

**Abstract.** Endometrial cancer in patients over 50 years old, compared with the group of 60-75 years old, is characterized by a predominance of high-grade carcinomas (27.2% versus 12%,  $p < 0.001$ ) due to the prevalence of non-endometrioid tumor histotype (16.98% versus 4.7%,  $p = 0.005$ ). Extensive forms of the disease (FIGO stages III-IV) among women aged  $\geq 70$  years were observed in 17.6% of cases versus 6.7% in the comparison group ( $p = 0.003$ ). The studied age groups were comparable in the extent of surgical treatment ( $p = 0.637$ ) and adjuvant therapy performed in the postoperative period ( $p = 0.749$ ).

**Keywords:** morphology, endometrioid adenocarcinoma.

**Relevance.** Population aging is the result of demographic changes, shifts in fertility and mortality patterns, and their ratios [1,3,5,7,9]. According to international criteria, a population is considered old if the proportion of individuals aged 55 and older exceeds 7% of the total population. According to statistics as of January 1, 2024, in Uzbekistan, 16% of the population, i.e., one in seven residents, is aged  $\geq 55$  years, and women account for 66.5% of the population in this age group [2,4,6,8,10].

Increasing life expectancy leads to an increase in the incidence of cancer among the elderly, which is a pressing issue in modern oncology. This issue requires a multidisciplinary approach, with mandatory implementation of a comprehensive geriatric assessment (CGA) to predict immediate and long-term treatment outcomes and select the optimal strategy, taking into account physical and mental status, social relationships, and satisfaction with quality of life [3,11].

Age is often a fundamental factor influencing treatment decisions for elderly cancer patients.

The results of a UK study assessing healthcare providers' biases in treating elderly breast cancer patients demonstrated that survey participants were significantly less likely to offer surgical treatment to older patients – 3% less likely for those over 50 years of age (compared to those aged 60), and 26% less likely for those aged 65 years. Thus, older age was a significant predictor of the decision to forgo surgical treatment. Survey data also revealed that age was not a primary consideration among respondents, but was frequently mentioned alongside factors such as comorbidities, tumor biology,

and reasons for avoiding surgery. Furthermore, there were responses indicating that there were cases in which older age was a clear factor for prescribing hormonal therapy over surgery, in contrast to younger patients, where the opposite was true. Some participants noted that treatment effectiveness is less important for older patients [1,13].

EC occupies a leading position in the structure of oncopathology in the female population [1, 14], with no potential for decline [2,15]. This is due to the increase in significant risk factors, particularly the ongoing aging of the population and obesity [60]. This creates the preconditions for an increase in the number of patients with a primary diagnosis of EC in the age group over 50 years.

A review of the literature revealed no studies in the domestic literature devoted to the clinical and morphological characteristics and long-term treatment outcomes of endometrial cancer in elderly and senile patients. Most foreign publications focus on the surgical aspects of treating patients in these age groups [3, 14].

Given that endometrial cancer treatment methods have changed significantly over the past 10 years and continue to change with the discovery of four molecular genetic variants of these tumors [14], the creation of an age-stratified registry of endometrial malignancies, taking into account new knowledge, will enable the development of unified clinical guidelines for this complex group of elderly patients.

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 Kharez 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. The results of the univariate analysis of qualitative variables influencing 5-year overall survival are presented in Table 38. Parameters that demonstrated statistical significance were then included in a multivariate regression analysis using the Cox proportional hazards model with stepwise inclusion of predictors. Factors influencing 5-year overall survival were as follows: age  $\geq 70$  years was associated with a 6.98-fold increased risk of death within 5 years, the p53abn molecular subgroup was associated with a 4-fold increased risk, and invasion of  $> 1/2$  myometrium was associated with a 3.03-fold increased risk.

These values were included in the prognostic model. The regression model was statistically significant ( $df = 3$ ;  $\chi^2 = 35.08$ ;  $p < 0.0001$ ). The area under the receiver operating characteristic curve (ROC) was  $0.841 \pm 0.038$  with a 95% CI of 0.772–0.895, indicating good discrimination between the presence and absence of risk for these factors in the studied cohort. The Harrell's C-index was 0.810 with a 95% CI of 0.751–0.870, indicating high predictive power of the resulting 5-year mortality risk model. The results of the univariate analysis of the qualitative indicators associated with 5-year EC recurrence are presented in Table 40. The indicators that demonstrated statistical significance were then included in a multivariate regression analysis using the Cox proportional hazards model with stepwise inclusion of predictors. The p53abn subgroup was characterized by a significantly increased risk of 5-year EC recurrence (2.49-fold), cervical invasion (2.9-fold), the presence of LVI (4.57-fold), and dissemination of the pathological process through the peritoneum (3.96-fold). Including age group in the multivariate analysis demonstrated a trend toward statistical significance ( $p = 0.0571$ ) in the increased risk of disease recurrence over 5 years. The area under the receiver operating characteristic (ROC) curve was  $0.825 \pm 0.036$  with a 95% CI of 0.757–0.880, indicating good discrimination between the presence and absence of risk for these factors in the studied cohort. The Harrell's concordance index (Harrell's C-index) was 0.773 with a 95% CI of 0.714–0.832, indicating good predictive performance of the resulting model for 5-year recurrence risk. According to our study, endometrial cancer in women over 70 years of age was characterized by a predominance of high-grade carcinomas, which were observed in every third patient ( $p < 0.001$ ), due to the prevalence of non-endometrioid neoplasms (16.98%) with a predominance of the serous histotype (7.55%) in their structure ( $p = 0.005$ ). A similar distribution of the morphological structure of malignant endometrial neoplasms was demonstrated by researchers from Israel, who studied the effect of age on endometrial cancer outcomes ( $\leq 80$  years vs.  $> 80$  years). In the group of older patients, high-grade carcinomas were recorded in 45% of cases due to the predominance of serous tumors (17%), while in the comparison group, similar figures were 27% and 15%, respectively ( $p = 0.018$ ) [15].

**Conclusions.** Thus, the study demonstrated that endometrial cancer in patients over 50 years of age is more aggressive based on the histological type of the tumor, its degree of differentiation, and the stage of the disease at diagnosis. Despite the absence of significant differences in the extent of surgical treatment and postoperative adjuvant therapy, the disease is characterized by worse long-term outcomes among older patients, as evidenced by statistically lower survival rates compared to patients aged 50-69.

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