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Forecast Factors in Patients with Uterine Cancer

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ABSTRACT

The prognosis for uterine cancer and the survival rate of patients largely depend on the stage of the disease, determined on the basis of intraoperative findings and histological examination results. Unfavorable prognosis factors that statistically significantly affect the long-term results of treatment of patients with uterine cancer of clinical stages I-III are the stage, age, depth of myometrial invasion, the degree of differentiation and size of the tumor, the presence of tumor emboli in the blood and lymphatic vessels of the myometrium, tumor cells in abdominal flushes, dissemination and lymphogenic metastases. Lymph node metastases are the most important prognostic factor for early-stage uterine cancer.

KEYWORDS: uterine cancer, prognostic factors, lymphogenic metastases, long-term treatment outcomes, overall survival, relapse-free survival.

The results of treatment refute the traditional idea of a favorable clinical course of uterine body cancer (RTM). Thus, the 5-year overall survival of patients with RTM stages I and II is 82 and 65%, respectively, and progression occurs in 25% of patients treated for early-stage RTM [5,12]. In the world, RTM ranks 4th in the structure of morbidity of women with malignant neoplasms and 7th in the structure of mortality from them. RTM is more common in pre - and postmenopausal women (75%), but in recent years there has been a tendency to rejuvenate patients with RTM. Significant rates of increase in the incidence of RTM are observed in the age groups of 40-49 (by 12.3%) and 50-56 years (by 15.6%) [2,7,22]. The prognosis for RTM and survival of patients largely depend on the stage of the disease, determined on the basis of intraoperative findings and histological examination results [3,25]. This takes into account the depth of myometrial invasion, the condition of the appendages and cervix, the results of revision of the abdominal cavity and small pelvis, biopsies of all suspicious volume formations and enlarged pelvic and paraaortic lymph nodes [1,12]. The data of preoperative examination and the clinical stage established on this basis do not coincide with the surgical findings and the results of histological examination in 51% of patients with RTM [4,8,10]. Thus, in RTM, it is optimal to determine the morphological stage of the disease. The risk of RTM metastases in regional lymph nodes, as well as disease progression, is primarily determined by the degree of tumor differentiation and the depth of myometrial invasion. Unfavorable prognostic factors for RTM are the presence of cancer emboli in the lymphatic slits, the transition of the tumor to the isthmus or cervix, the absence of estrogen and progesterone receptors in the tumor, a large primary tumor, the presence of K-ras mutations, and the superexpression of ERBB2 and p53 [6,12,22]. Lymph node metastases are the most important prognostic factor in early-stage RTM. For a long time, there has been a scientific debate about the volume of surgical interventions for RTM. This problem has two aspects: the expediency of expanding their volume, taking into account the

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characteristics of the lymphogenic metastasis and the possibility of performing extended operations in patients who usually suffer from severe endocrine-metabolic disorders and concomitant diseases of the cardiovascular system. There are different methods of visual and morphological assessment of the condition of regional lymph nodes in RTM: ultrasound, palpation and biopsy of enlarged lymph nodes, biopsy of one enlarged lymph node, selective and total lymphadenectomy. Unfortunately, there are still no uniform FIGO recommendations for determining the morphological stage of RTM. Taking into account the above, the aim of the study was to study the effectiveness of three methods of combined treatment of RTM, identify prognostic factors and develop evidence-based recommendations for performing extended operations for RTM. The study included 395 patients with stage IA— IIIC RTM aged 30-89 years who were treated at the N. N. Blokhin Russian Cancer Research Center of the Russian Academy of Medical Sciences from 1995 to 2005. The diagnosis in all patients was established for the first time based on the results of histological examination. The average age of patients amounted to 60.4±0.5 years: 15 (3.8 per cent) before the age of 40 years, 37 (9,4%) — aged 40-49 years, 143 (36.2%) in the age of 50-59 years, 137 (34,7%) in the age of 60-69 years, 63 (15,9%) at age 70 years and older. Thus, the vast majority of patients with RTM (343 patients, 86.8%) were aged 50 years and older. All patients were followed up for 1 to 10 years. The five-year overall survival rate of patients with RTM stages I—III was 75.9±2.6%, 10-year overall survival rate was 71.5±3.2%, and 5 — year relapse-free survival rate was 71.3±3.1%. The stage of the disease is statistically significantly associated with the prognosis of patients with RTM ($p = 0.00001$). Thus, 81.3% of patients with stage I disease were observed for 5 years without signs of disease progression. The ten-year survival rate of patients in this group was 77.1±3.3%. At stage III of the disease, 50% of patients died from relapses and distant metastases within 42.5 months, and 25% of patients died within 20.8 months. There were no statistically significant differences in the long-term results of treatment in patients with RTM stages IIA and IIB, IIIA, IIIB and IIIC ($p >> 0.05$). The five-year overall survival rate of patients with RTM stages IIIA-IIIC is statistically significantly lower than that of patients with RTM stages IA-IC ($p = 0.0001$) and IIA—IIB ($p = 0.01$). Similar results were found in the study of relapse-free survival in patients with RTM. Thus, 5-year relapse-free survival in patients with stage I RTM was 80.5±2.1%, stage II-69.8±7.9%, stage III-41.9±11.3% ($p = 0.00001$). The median disease-free period in stage III RTM was 27.9 months. The five-year overall survival rate for RTM T1N0M0 is statistically significantly higher than for RTM T1N1M0 (81.3±2.8 and 30.9±17.9%, respectively, $p = 0.001$). Due to the small number of patients with T2a—3bN1 tumors, treatment results in this group were not compared depending on the presence of lymphogenic metastases. However, it should be noted that in the presence of regional lymphogenic metastases, the 5-year survival rate of patients was less than 50%. In T3a tumors, the 5-year survival rate of RTM patients with and without metastases was comparable. Statistically significant differences were found in the study of long-term results of treatment of patients with RTM of different age groups. It was found that the 5-year survival rate of patients older than 60 years is statistically significantly lower than in other age groups (p Similar trends were observed in the analysis of 5-year relapse-free treatment. survival rate. So, in patients under 40 years of age, it was 87.9±13.5%, 40-49 years-88.1± 5.8%, 50-59 years-78.6±3.9%, 60-69 years-61.8±5.4%, 70 years and older-50.1±8.4%. The five-year overall survival rate of patients with clear cell RTM is lower than that of patients with other histological types of RTM ($p = 0.04$). The fiveyear disease-free survival rate of patients with endometrial adenocarcinoma was

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72.5±3.6%, endometrial adenocarcinoma with squamous cell metaplasia-81.0±4.8%, and clear cell cancer-47.7±9.4% (p = 0.038). The median disease-free period was 51.9 months. Out of 5 patients with mixed RTM, 2 patients died from disease progression at 3 and 9 months, 3 patients continue to be observed (29, 72 and 108 months). Of the 3 patients with papillary serous RTM, 1 patient died 44 months after treatment from disease progression, 2 were observed at 72 and 93 months. One patient with squamous cell RTM was observed for 42 months without signs of disease progression. Long-term results of treatment of patients with highly differentiated endometrial adenocarcinoma stages I-III are better than long-term results of treatment of patients with RTM with moderate, low and mixed differentiation (p = 0.04). Long-term treatment outcomes for moderate, grade, low-grade adenocarcinoma and mixed-grade adenocarcinoma did not differ statistically (p > 0.05). The five-year disease-free survival rate of patients with endometrial adenocarcinoma stages I—III was 91.4±3.8% with high tumor differentiation, 70.1±5.4% with moderate принизкойdifferentiation, 65.3±10.9% with low differentiation, and 65.2±7.9% with mixed differentiation (p = 0.04). When analyzing the 10-year overall survival rate depending on the depth of myometrial invasion, it was noted that it was greatest when less than half of the myometrial thickness was sprouted (80.9±3.4%). The results of treatment of patients in whom the tumor sprouted more than half the thickness of the myometrium, and patients in whom the tumor sprouted to the serous membrane, were the same. Both patients with uterine serous membrane tumor growth died from disease progression in 9 and 10 monthsHistological examination revealed no myometrial invasion in 11 patients. At the same time, metastases in regional lymph nodes were detected in 2 patients, and the transition of the tumor to the cervix — in 1. Overall, survival in this group was low and amounted to 18.2±1.3%, due to a combination of unfavorable prognosis factors. The five-year disease-free survival rate of RTM patients, depending on the depth of myometrial invasion, was 81.3±2.9% when the tumor sprouted less than half the thickness of the myometrium and 62.8±5.9% when the tumor sprouted more than half the thickness of the myometrium (p = 0.000001). There was a tendency to worsen the long-term results of treatment in patients with RTM with a transition to the cervical stroma compared to those in patients with a transition of the tumor to the cervical canal mucosa (5-year overall survival of 55.9±10.1 and 74.6±6.6%, respectively, p = 0.08). The five-year relapse-free survival rate of patientswith during the transition of the tumor to the cervical mucosa was 71.3±9.3%, to the stroma-52.1±19.8% (p = 0.061). Tumor emboli in the blood and lymphatic vessels of the myometrium significantly worsen the long-term results of treatment of patients with RTM (p = 0.035). The five-year overall survival rate of patients with RTM, depending on the presence of tumor emboli, did not differ significantly, while the 10-year overall survival rate had significant differences (p = 0.013). Five-year relapse-free treatment The survival rate of patients with RTM was 59.3±9.4 and 75.7±3.3%, respectively (p = 0.049). Based on the results of our study, there is a tendency to reduce the survival rate of patients with RTM with ovarian metastases. The five-year disease-free survival rate in the presence of ovarian metastases was 68.6±16.8%, in the absence of metastases-81.8±2.5% (p = 0.35). Regional lymphogenic metastases, according to our data, are one of the most significant factors of unfavorable prognosis, statistically significantly affecting the survival of patients. A quarter of RTM patients with regional lymph node metastases died of disease progression within 20 months, and half died within 44.5 months. The five-year overall survival of RTM patients with and without regional lymph node metastases was 47.6±11.7 and 82.0±6.3% (p = 0.0018), the 5-year relapse-free survival was 41.3±12.1 and 80.9±6.9%

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(p = 0.01), and the median relapse — free period was 30.8 months. Peritoneal dissemination significantly reduces long-term treatment outcomes in patients with RTM (p = 0.00005). A quarter of patients in this group died of disease progression within 9.6 months. The median life expectancy of patients in this group was only 21.6 months, while in the group of patients without peritoneal dissemination it was not achieved. The five-year overall survival of RTM patients with and without peritoneal tumor dissemination was 28.7±17.0 and 77.6±2.6% (p = 0.0025), the 5-year relapse — free survival was 24.3±16.8 and 75.4±3.2% (p = 0.00016), and the median relapse — free period was 12.5 months. Statistically significant differences in the survival rate of patients with RTM were found depending on the size of the primary tumor. The 5-year relapse — free survival rate was 61.4±5.2% for primary tumors larger than 4 cm, and 78.9±3.8% for tumors smaller than 4 cm (p = 0.018). There was a tendency to improve the 10-year overall survival of patients with tumors containing progesterone receptors, and to worsen the 5-year overall survival of patients with tumors without estrogen and progesterone receptors (p = 0.25). Five-year relapse-free survival in patients with EB, depending on the receptor status of the tumor did not differ and was in the group of patients with receptormediated tumors 54,3±11,0%, with tumors containing only progesterone receptors, — 69,8±12.6%, and with tumors containing only estrogen receptors, which is 65.4±12.9 percent, with receptorpositive tumors is 68.5±8.1 percent. The analysis showed statistically significant differences in the long-term results of treatment of patients with RTM, depending on the presence of tumor cells in the abdominal flushes (p = 0.0001). Thus, in the absence of tumor cells in the flushes, the median life expectancy of patients was not reached, and in the presence of tumor cells, it was 26.7 months. The five-year overall survival rate was 77.4±2.6% and 30.5±15.0%, respectively (p = 0.00001). The five-year disease-free survival rate of RTM patients was 84.1±2.7% in the absence of tumor cells in the washouts, 26.5±15.7% in the presence of tumor cells in the washouts (p = 0.00012), and the median disease — free period was 19.7 months. Thus, the factors of unfavorable prognosis that statistically significantly affect the long-term results of treatment of patients with RTM of clinical stages I-III are the stage, age, depth of myometrial invasion, the degree of differentiation and size of the tumor, the presence of tumor emboli in the blood and lymphatic vessels of the myometrium, tumor cells in abdominal flushes, dissemination, and lymphogenic metastases.

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