



Diagnosis and Treatment of Recurrent Breast Cancer Glands

1. Khalikova Feruza Sharofovna
2. Sokhibova Ziyoda Rakhmonovna

Received 2nd Jun 2022,
Accepted 3rd Jul 2022,
Online 30th Aug 2022

^{1,2} Bukhara State Medical Institute,
Assistant of the Department of Oncology
and Medical Radiology

Abstract: The problem of breast diseases (MG) remains relevant not only in Uzbekistan, but throughout the world, since the prevalence of both benign and malignant lesions of the breast is growing everywhere. Recently, many authors note that there is a rejuvenation of the contingent of patients with breast cancer [1,11,7]. In this regard, 30% of women with detected tumors are under the age of 40, when benign proliferative diseases of the breast are most often detected. In the structure of the incidence of malignant tumors in the world, breast cancer ranks third after lung and stomach cancer, accounting for 10% of all morbidity. About one million women develop breast cancer every year.

Key words: breast, breast cancer, postmenopause, hyperestrogenemia.

INTRODUCTION. In the structure of malignant tumor mortality in the world, breast cancer ranks sixth, after cancer of the lung, stomach, colon and colon, and liver, which accounts for 6% of all malignant tumor deaths [12]. In the regions of Kyrgyzstan, the incidence varies from 14 to 2 per 100,000 population in Chui oblast to 1.8 in Batken oblast. It is noteworthy that in Bishkek this figure is 22.0. In the structure of mortality from malignant neoplasms, breast cancer also ranks third (4.1%) after gastric cancer and lung cancer (11% and 7.7%, respectively) [15]. The choice of a method for treating breast cancer is determined by the stage of the disease, the clinical form of the tumor, the age and general condition of the patient, as well as additional data that characterize the individual properties of the tumor and the patient's body (hormonal, immune, and others). According to other data, 9-17% of patients develop local recurrences within 10 years [30,81]. The five-year recurrence-free survival rate for patients with medial localization of the tumor is 66.3%, and for patients with lateral localization - 74.2% [76]. The risk of recurrence within 10 years in breast cancer corresponding to T1N0M0 with a tumor size of 1 cm to 2 cm is 25%, and with T2N0M0 it reaches 30-35% [16]. The ambiguity of data on the frequency of breast cancer recurrence, differences in causative factors often lead to an inadequate assessment of the condition of patients, and sometimes they are considered hopeless. Nevertheless, in all cases it is necessary to apply medicinal, radiation and surgical methods, to achieve remission and stabilization of the disease. The treatment of relapses is a very difficult task, on the one hand due to the tendency to rapid dissemination, and on the other hand, due to the fact that

a certain part of the body's reserves, in the broad sense of the word, have already been exhausted during the treatment of the primary lesion. Attempts were made to standardize therapeutic measures depending on the above factors, as well as the development of an individual approach to solving problems in the treatment of relapses in each case. The effectiveness of one or another therapeutic method has not been sufficiently clarified, and the determination of the tactics of therapeutic measures and their results in relapses is of certain theoretical and practical interest. The above factors determined the relevance and expediency of this study.

Purpose of the study: improving the results of treatment of patients with recurrent breast cancer.

Material and methods: The material for the present study was clinical data on 178 patients who received treatment for local recurrence of breast cancer at the National Oncology Center of the Republic of Uzbekistan from 2019 to 2022. For data analysis, a codifier was compiled, including 91 features, with their gradations. The content of the case histories and outpatient cards were processed according to the codifier and put on punched cards of the K-5 type with marginal perforation. At the end of the study, the obtained clinical data were transferred and processed using the Microsoft XP software package. In accordance with the goal and objectives, the studied patients were divided into groups: 1. The first group - the study group consisted of 30 (16.5%) patients who received complex treatment (surgery, radiation therapy, chemo-hormonal treatment) for breast cancer recurrence. 2. The second group consisted of 67 (36.8%) patients who received combined treatment (surgery or radiation therapy in combination with chemotherapy) 3. The third group consisted of 30 (16.5%) patients who received only local treatment (surgery and /or radiation therapy) for recurrence of breast cancer. 4. The fourth group included 55 (30.2%) patients who received systemic treatment (chemo-hormone therapy) for breast cancer recurrence. Such a division into groups made it possible to study not only the results of various methods of treating breast cancer relapses, but also to conduct a comparative analysis of them with each other in order to determine the effectiveness of the treatment. The significance of the following prognostic factors was assessed: the reproductive status and age of the patients, the histological structure of the primary tumor at the time of surgical treatment, its prevalence and treatment methods. The age of the patients varied from 24 to 84 years. The mean age of patients with relapses was 53.6 years. The most significant number of patients with recurrence of breast cancer were patients in the menopausal period 127 (69.8%), and the absence of menopause was in 55 (30.2%) women (Table 1). The average time for recurrence was 34.8 $\pm$ 5.4 months. and 17.3 $\pm$ 4.3 months. ($p < 0.01$), respectively.

Table 1. Distribution of patients by age and menstrual status

Menstrual status	Age group												Total	
	<29		30-39		40-49		50-59		60-69		>70			
	a6c.	%	a6c.	%	a6c.	%	a6c.	%	a6c.	%	a6c.	%	a6c.	%
Absence of menopause	2	1,1	15	8,2	30	16,5	8	4,4	-	-	-	-	55	30,2
Presence of menopause	-	-	4	2,3	23	12,6	44	24,2	31	17,0	25	13,7	127	69,8
Total	2	1,1	19	10,5	53	29,1	52	28,6	31	17,0	25	13,7	182	100

An important biological criterion that reflects the characteristics of the clinical course of breast cancer is its histological structure. According to some authors, the rate of tumor growth, the degree of invasiveness, and the tendency to metastasis depend on the histological structure of the tumor, and the prognosis of the disease is also largely determined [10]. Therefore, the morphological identification of breast cancer is of great practical importance in addressing issues of treatment tactics. Ductal and lobular infiltrating breast carcinomas accounted for 61.0% (34.0% and 27.0%, respectively). This

system of gradation according to the degree of malignancy is based on the degree of structural and cellular atypism, on the severity of proliferative processes, determined by the number of mitotic figures. Highly differentiated malignant tumors of the mammary gland Gb, moderately differentiated G2 and poorly differentiated G3, were identified. The proportion of patients with relapses was 35.2% for G3, 25.3% for G2, and 1.1% for G\ . The terms of recurrence were 23.4 $\bar{I}$ } 2.7 months, 31.3 $\bar{I}$ } 3.2 and 41.5 $\bar{I}$ } 3.6, respectively (relative to Gi p<0.05 for G2 and G3). If patients underwent neoadjuvant treatment at the preoperative stage, then the severity of therapeutic pathomorphosis is important as a prognostic factor. For the morphological assessment of the degree of damage to tumor cells, the generally accepted classification was used: with degree I damage, no noticeable changes in the overall structure of the tumor could be noted. At grade II, foci of regressive changes are clearly observed on histotopographic sections, although the bulk of the tumor remains. The third degree is characterized by a sharp violation of the structure of the tumor due to the replacement of its parenchyma with fibrous tissue or extensive necrosis. At IV degree - complete disappearance of tumor elements. Patients with recurrent breast cancer who had therapeutic pathomorphosis accounted for 32.9%. Moreover, I degree was detected in 17.0% of patients and the average time for the appearance of relapse was 19.9 $\bar{I}$ } 3.8 months. With the II degree of therapeutic pathomorphosis, the number of patients was 10.4% and the average time for the onset of relapse was 32.3 $\bar{I}$ } 4.2 months. The third degree was revealed in 5.5% and the average time for the appearance of relapse was 38.5 $\bar{I}$ } 5.1 (relative to the I degree of therapeutic pathomorphosis, p<0.05 for the II degree and p<0.01 for the III degree). Other histological types of breast cancer such as medullary, mucosal, squamous, apocrine, and Paget's cancer accounted for 5.0% and the mean recurrence time was 37.9 $\pm$ 1.6 months. Non-invasive Tis breast cancer was found in 1 patient (0.5%) and the period of occurrence of recurrence was more than 10 years. The distribution of patients with relapses of breast cancer, depending on the degree of prevalence of the primary tumor in accordance with the International classification according to the TNM system (2002) is presented in Table 2. At stage I (TiN0Mo) the number of patients was 7 (3.9%) people and the average period of recurrence was 39.8 $\bar{I}$ } 4.8 months. With the Pa stage (To-iNiMo and T2NoM0), 23 (12.7%) patients were identified, the average relapse time was 36.7 $\bar{I}$ } 4.1 months. A H stage 6 (T2NiM0 and T3N0M0) was in 36 (19.7%) patients and the average relapse time was 33.2 $\bar{I}$ } 3.7 months. The stage of the process classified as Sha (T0-1N2M0 and T3Ni.2M0) was determined in 47 (25.8%) patients and the average time for the appearance of relapse was 26.3 $\bar{I}$ } 2.9 months. At stage III6 (T4NnioGMo and T^6.N3Mo), the number of patients was 68 (37.4%) and the average relapse time was 16.9 $\bar{I}$ } 2.2 months (relative to stage I pP0.05 for Ia and IIb and p<0.05 for IIIa and III stages).

Non-invasive cancer, i.e. O stage was found in 1 (0.5%) patient.

Table 2. Distribution of patients with relapses, depending on the degree of prevalence of the primary tumor

Primary tumor	Status of regional lymph nodes								Total	
	N0		N1		N2		N3			
T	abs.	%	abs.	%	abs.	%	abs.	%	abs.	%
Tis	1	0,5	-	-	-	-	-	-	1	0,5
T1	7	3,9	3	1,7	-	-	-	-	10	5,6
T2	20	11,0	15	8,2	9	5,0	-	-	44	24,2
T3	21	11,5	23	12,6	15	8,2	-	-	59	32,3
T4	8	4,4	26	14,3	34	18,7	-	-	68	37,4
Total	57	31,3	67	36,8	58	31,9	-	-	182	100,0

With the prevalence of the tumor process, designated as T4, the greatest number of relapses was noted - 37.4%, with T3 this figure was 32.3%, with T2 - 24.2%, with Tj only 5.6%. We identified one case of local recurrence in TjS, which accounted for 0.5% of the total number of patients with recurrent breast cancer. At the same time, the rate of development of relapses increased in direct proportion to the prevalence of the primary tumor process, and if with Tis the recurrence of breast cancer occurred after more than 10 years, then with Ti the average time for the onset of recurrence was 38.8 $\bar{1}$ }4.6 months, with T2 - 30.1 $\bar{1}$ }3.9 months, at T3 19.5 $\bar{1}$ }3.4 months and at T4 16.9 $\bar{1}$ }2.2 months (relatively $p < 0.05$ for T2 and $p < 0.001$ for T3 and T4).

An important prognostic sign is the presence of metastatically affected lymph nodes. The number of patients with lymph node metastases was 125 (68.7%), without them - 57 (31.3%). The average time for the appearance of recurrence was significantly higher for the second category and amounted to 41.6 $\bar{1}$ }5.8 months, versus 26.5 $\bar{1}$ }4.4 for the first ($p < 0.05$). According to the methods of treatment of the primary tumor, all patients were divided into 3 groups: those who received complex treatment (surgery, chemohormonal and radiation therapy) - 131 (72.1%) patients, combined treatment (surgery and either radiation therapy or chemohormonal therapy) - 45 (24.7%) and patients who underwent only surgical treatment - 6 (3.2%) patients (Table 3).

Table 3. Scope of treatment and tumor stage

Treatment	Stage												Total	
	0		I		IIA		IIB		IIIA		IIIB			
	abs.	%	abs	%	abs	%	abs.	%	abs.	%	abs.	%	abs.	%
Comprehensive	-	-	1	0,5	14	7,7	29	16,0	39	21,5	48	26,4	131	72,1
Combined	1	0,5	6	3,3	12	6.6	5	2,8	4	2,2	17	9,3	45	24,7
Surgical	-	-	-	-	1	0,5	1	0,5	1	0,5	3	1,7	6	3,2
Total	1	0,5	7	3,8	27	14,8	35	19,3	44	24,2	68	37,4	182	100

Most of the patients (72.1%) received complex treatment for the primary tumor, and the average recurrence time was 32.3 $\bar{1}$ }3.4 months. Combined treatment was carried out in 24.7% of patients and the average period of recurrence was 27.0 $\bar{1}$ }3.5 months. Only surgical treatment was provided to 3.2% of patients who had certain contraindications for chemoradiotherapy, and the rate of recurrence was the highest 14.2 $\bar{1}$ }3.1 months. Additional irradiation increased the period of recurrence to 30.4 $\bar{1}$ }3.7 months ($p < 0.001$), and adjuvant chemohormonotherapy to 23.6 $\bar{1}$ }3.2 months ($p < 0.05$). 3 months. The distribution of patients depending on the duration of the relapse-free interval is shown in Fig.3. The largest number of relapses was detected during the first year of observation - 41.2%, in the second - 25.8%, in the third and fourth years of observation, the number of relapses was 14.3% and 9.9%, respectively. In terms of five years or more, relapses were found in 8.8% of patients.

Of the total number of patients, 104 (57.1%) had single recurrent nodes, and 78 (42.9%) had multiple lesions. In 16 (8.8%) patients, the disintegration and ulceration of the recurrent node was revealed, in 21 (11.5%) the recurrence had an infiltrative growth pattern, spreading to a significant part of the chest wall like shell cancer. At the same time, the period of appearance of single and multiple formations turned out to be almost the same, however, it was significantly lower for relapses of lymphangitis: 31.6 $\bar{1}$ }6.8 and 28.3 $\bar{1}$ }4.6 months versus 9.2 $\bar{1}$ }5.4 months, respectively ($p < 0.01$). Local recurrences were subdivided according to spatial and tissue affiliation into: 1. local (in the area of the postoperative scar, the anterior surface of the chest wall on the side of the primary tumor). The number of patients was 121 (66.5%). The average time for the appearance of a relapse was 28.3 $\bar{1}$ }3.8 months; 2. regional (in the axillary, supraclavicular, cervical, parasternal lymph nodes on the affected side). The number of patients was 30 (16.5%). relapses in the mammary gland after organ-preserving treatment. The number of patients was 31 (17.0%).

CONCLUSION

Scientists and doctors are trying with the help of new methods of treatment, new approaches, new drugs to find the best way to influence the disease. Perhaps, none of the localizations of cancer can be considered as difficult to choose a rational and adequate treatment as breast cancer. This is due to the extraordinary variety of options for the clinical manifestation and course of the disease and, therefore, the need to take into account many factors when planning treatment, any of which can be decisive in the prognosis of the disease and, accordingly, the fate of the patient. The surgical method remains the main therapeutic effect, and the outcome of the disease largely depends on the quality of its implementation, and inadequate local treatment leads to an increased risk of local recurrence and reduced survival. Therefore, local-regional control is a “zone of increased interest” of oncologists. The material for the study was data on 182 patients who received treatment for breast cancer recurrence in the period from 2019 to 2022. The significance of the following prognostic factors was assessed: reproductive status and age of patients, the histological structure of the primary tumor at the time of surgical treatment, its prevalence and methods of treatment. The age of the patients varied from 25 to 83 years. The mean age of patients with relapses was 53.5 years. In 55 (30.2%) women, the absence of menopause was noted, and in 127 (69.8%) menopausal age, and in 52 menopause was induced during the treatment of the primary tumor (ovariectomy was performed). In young women and in women in early menopause, more aggressive forms of breast cancer occurring with rapid dissemination of the process are more often detected. The rate of its growth, the degree of invasiveness and the tendency to metastasis depend on the histological structure of the tumor, and the prognosis of the disease is also largely determined. Patients with breast cancer recurrence, who had grade I therapeutic pathomorphism in the treatment of the primary tumor, accounted for 17.0% and the average recurrence time was 19.9 ± 0.8 months. With the II degree of therapeutic pathomorphosis, the number of patients was 10.4% and the average time for the onset of relapse was 32.3 ± 4.2 months. The third degree was revealed in 5.5% and the average time for the appearance of recurrence was 38.5 ± 5.1 months (in relation to the I degree of therapeutic pathomorphosis, $p < 0.05$ for the II degree and $p < 0.01$ for the III degree). If tumor cell damage is minimal after neoadjuvant treatment, then such patients develop relapses of breast cancer more often and faster. % and the average period of recurrence was 37.9 ± 11.6 months, i.e. there is a more indolent course of these forms of breast cancer. Non-invasive form of breast cancer Tis was found in 1 patient (0.5%) and the period of recurrence was more than 10 years. The degree of prevalence of the primary breast tumor is important in predicting the process of recurrence. An important prognostic sign is the presence of metastatically affected lymph nodes. The proportion of patients with lymph node metastases was 125 (68.7%), without them 57 (31.3%). The average period of recurrence was significantly higher for the second category and amounted to 41.6 ± 5.8 months versus 26.5 ± 4.4 for the first ($p < 0.05$). At stage I (T1N0M0), the number of patients was 7 (3.9%) people and the average time for the onset of relapse was 39.8 ± 4.8 months. With stage Ia (T0.1N1M0 and T2N0M0), 23 (12.7%) patients were identified, the average relapse time was 36.7 ± 4.1 months. A I I b stage (T2N1M0 and T3N0M0) was in 36 (19.7%) patients and the average period of recurrence is 33.2 ± 3.7 months. The stage of the process classified as Sha (T0.1N2M0 and T3N1.2M0) is defined in 47 (25.8%) patients and the average relapse time was 26.3 ± 2.9 months. At III6 stage (T1N1S1M0 and T1N1bM3M0), the number of patients was 68 (37.4%). and the average time for the appearance of relapse was 16.9 ± 2.2 months (relative to stage I $p > 0.05$ for -II* and I 6 $p < 0.05$ for PG and III6 stages). Non-invasive cancer, i.e. Stage 0 was found in 1 (0.5%) patient. In the study of the volume of treatment provided for the primary tumor, it was revealed that with complex treatment (surgery, chemo-, hormonal and radiation treatment), the average time of occurrence; recurrence was 32.3 ± 3.4 months. In 3 (1.7%) patients were found. metastases in deep groups of supraclavicular lymph nodes. Under m. sternocleidomastoideus and along the course of v. jugularis interna, a chain of inactive dense ones was palpated. lymph nodes. Metastasis to parasternal lymph

nodes was diagnosed in 4 (2.2%) patients. Clinically, it was defined as a clearly defined tumor, or diffuse induration without clear boundaries at a distance of 0.5–1.0 cm from the edge of the sternum, somewhat mobile in its protruding parts, and the base of the sprouting soft tissues of the intercostal space. Sometimes, on examination, a retraction of the skin and soft tissues was found in a limited area near the sternum. Palpation revealed an infiltrate without clear boundaries, located in the intercostal space, with fixation of the skin above it! Skin metastases were observed in 17 (9.3%) patients and were single or multiple. They appeared when the tumor spread through the lymphatic vessels located in the thickness of the skin or subfascially. Clinically, these are dense, rounded, painless reddish nodules in relatively close proximity to the surgical intervention area, rising above the skin level. Metastases in the area of the postoperative scar occurred in 121 (66.5%) There were 64 (35.2%) implantation recurrences that occurred with insufficient ablasticity of the operation, relapses 19 (10.4%) - with insufficient radicalism of the operation, when recurrence occurs in the surgical field itself, as well as lymphangic relapses 38 (20.9%), arising in the lymphatic tract, due to cancerous lymphangitis or cancerous emboli. Distinguishing metastases in the area of the postoperative scar, due to the occurrence, is necessary, because they have a different clinical course and prognosis. Implantation relapses were manifested as single nodes of various sizes (from 0.5 to 3.0 cm in diameter), reddish in color, dense, painless, rapidly ulcerating. They also formed far from the scar, for example, at the site of the incision for the drainage tube. Therefore, additional diagnostic methods are needed - instrumental and laboratory studies. Ultrasound examination made it possible to visualize and get an idea of the location, size of the tumor and the structure of the surrounding tissues, as well as to differentiate postoperative and post-radiation changes in soft tissues. The tumor was identified as a hypoechoic mass with an indistinct, often radiant contour. With a size of up to 1.0 cm, it had an almost homogeneous structure, in larger formations, anechoic cavities and hyperechoic inclusions appeared (in the form of small dots and convoluted lines or polygonal structures). The ultrasound picture in case of damage to regional lymph nodes was characterized by the following features: a bumpy outer contour, a heterogeneous structure due to areas of heterogeneous density, seals in the form of strands and scars, and the presence of liquid areas of various shapes and sizes. Using computed tomography, the prevalence of cancer recurrence was determined of the breast on the soft tissues of the anterior chest wall, destruction of bone structures, invasion into the anterior mediastinum, clarification of the spread to regional lymph nodes. The final step in any diagnostic search for breast cancer recurrence is a morphological study. Which establishes the morphological diagnosis of recurrence, the degree and nature of the spread of the process in the surrounding tissues and characterizes the receptor status of the recurrent tumor. Diagnosis of breast cancer recurrence should be based on a comprehensive and complete assessment of all clinical, laboratory, instrumental and morphological data. Only an integrated approach to the diagnosis of this pathology with a mandatory morphological study will allow developing an adequate treatment strategy and improve the immediate and long-term results of treatment. The aim of this work was to evaluate the effectiveness of treatment of patients with recurrent breast cancer, depending on the location of the recurrence and the approach to treatment (complex, combined, local and systemic). Local relapses, depending on the localization, are divided into: local, i.e. localized on the chest wall after radical mastectomy; regional - in the regional lymph nodes on the side of the lesion and relapses in the mammary gland after organ-preserving operations. The most favorable results of treatment of breast cancer relapses were obtained when the latter were localized in the mammary gland: 90.3 + 5.3% survived 1 year, 75.0 + 8.2% survived 3 years, 66.0 + 8% survived more than 5 years. .5% (in relation to local relapses $p < 0.01$). With regional relapses, almost the same survival rate was noted - 90.0 + 5.5% survived 1 year, 71.0 + 8.2% survived 3 years, 62.2 + 8.9% survived more than 5 years (in relation to local relapses $p < 0.05$). The overall survival rate for local relapses is the lowest - 68.6 + 4.2% survived 1 year, 39.9 + 4.5% survived 3 years, 37.5 + 4.4% survived more than 5 years. When a recurrence is localized in the mammary gland or in regional lymph nodes, the recurrent focus remains localized within the organ or lymph node for some time, and

with timely treatment, effective local control is provided. According to the methods of treatment for breast cancer recurrence, the patients were divided into 4 groups: the first study group consisted of 30 (16.5%) patients who received complex treatment (surgery, radiation therapy, chemo-hormonal treatment for breast cancer recurrence. The second group consisted of 67 (36.8%) patients who received combined treatment (surgery or radiation therapy in combination with chemohormonal therapy). The third group consisted of 30 (16.5%) patients who received only local treatment (surgery and / or radiation therapy) according to about the recurrence of breast cancer, and the fourth group included 55 (30.2%) patients who received chemohormonal therapy. In complex treatment, surgery was performed at the first stage, while the volume of surgical intervention varied from excision of the tumor with local and regional relapses, before amputation and radical mastectomy with relapses in the mammary gland. Postoperative complications were noted in 4 (13.3%) patients after Completion of radical mastectomy: in 3 patients - lymphorrhea, in the 1st - marginal necrosis of skin flaps. According to our data, it is advisable to use the surgical method for single mobile relapses in the area of the postoperative scar, as well as for relapses in the mammary gland after organ-preserving surgical treatment. At the second stage, the patients underwent radiation therapy on the same half of the chest and the area of regional metastasis. The interval between surgical treatment and radiation therapy was 2 weeks after tumor excision and 3-4 weeks after breast removal. Moreover, in the first case, the irradiation techniques were from wide-field to local, with equivalent total focal doses in the range of 24–36 Gy and irradiation modes up to 1 fraction of 4 Gy. After mastectomy, the method of radical radiation therapy was used with a single dose of 2–2.5 Gy and a total focal dose of 44–50 Gy. In 4 (13.3%) patients with a single dose of more than 3 Gy, complications developed in the form of post-radiation epidermitis. In parallel with radiation therapy, less often after it, patients underwent chemotherapy. Most often, patients were prescribed the CMF regimen (in 50.0% of cases), less often AC - 26.7%, CAF was prescribed in 23.3% of patients. More often, 4 courses of chemotherapy were performed - in 36.7% of cases, 3 courses were administered less frequently (23.4%). One and two courses were prescribed in 3.3% and 10.0%, respectively, which was caused by the presence of concomitant diseases in patients and their exacerbation during chemotherapy, 5 and 6 courses were administered with the same frequency of 13.3%. Side effects during chemotherapy were observed in 28 (93.3%) patients, the main ones were nausea, vomiting, neutropenia, leukopenia, diarrhea, stomatitis and alopecia. In the complex treatment of recurrence of breast cancer, hormone therapy was prescribed. It was carried out in patients with indirect signs of a hormone-dependent disease, which include advanced (postmenopausal) age, a long-term “mild” course of the disease, and predominant metastasis to soft tissues. Ovarian function was switched off in patients with preserved menstrual function with the help of luteinizing hormone releasing hormone (LHRH) agonists Zoladex - in 3.3% of cases, radiation castration - 3.3% and ovariectomy - 6.8%. In 3.3%, hormone therapy with androgen - sustanon was performed. Hormone therapy with progestin - medroxyprogesterone acetate was performed with the same frequency (3.3%). Most often, in 81% of cases, tamoxifen was used during hormone therapy. Patients who relapsed 12 months or more after discontinuation of tamoxifen therapy for the primary tumor retained a chance of responding to re-treatment with this drug. Patients who relapse during treatment with tamoxifen or less than 12 months after its discontinuation have "anti-estrogen-resistant" tumors and were treated with alternative approaches (aromatase inhibitors, androgens, progestins). The main side effects observed with the use of hormonal drugs were such as hot flashes, edema, hypertrichosis, acne, hoarseness, increased blood pressure, thrombotic complications, uterine bleeding, weight gain, headache, gastrointestinal tract disorders. With the localization of recurrence in the mammary gland after organ-preserving operations, 5 (7.5%) patients underwent surgical treatment in the amount of amputation of the mammary gland with axillary lymph node dissection. Two (3.0%) patients underwent radiation therapy according to the radical program with conventional fractions (total focal dose - 44 Gy, single dose - 2 Gy). In case of regional relapses, 2 (3.0%) patients with metastases in the ipsilateral axillary lymph nodes underwent axillary lymph

node dissection. In the remaining 15 (22.4%) patients, the supraclavicular lymph nodes on the side of the primary tumor were affected (the diagnosis was confirmed by cytological examination) and they underwent radiation therapy. Total focal doses varied from 25 to 50 Gy, single doses from 2 to 4 Gy. At the same time, a complication in the form of radiation epidermitis was noted in 4 (6.0%) patients with a single dose of more than 3 Gy. Chemotherapy was carried out after surgical treatment or in parallel with radiation therapy. The most frequently used scheme was CMF in 32.8% of cases, less often CAF - in 26.8%. AC and FEC schemes - in 19.4% and 13.5%, respectively. Monochemotherapy (doxorubicin or taxotere) was used in 7.5% of patients with recurrent breast cancer. One and two courses were received by 3.0% and 7.5% of patients, and due to poor tolerance and the absence of signs of disease progression, they refused further courses. Three (13.5%) and four (20.9%) courses were also limited in severe side effects and exacerbation of concomitant diseases. Most often, patients received 5 (23.9%) and 6 (26.7%) courses of chemotherapy. Side effects during chemotherapy were observed in 57 (85.1%) patients. There were gastrointestinal disorders (nausea, vomiting, diarrhea) - in 32 (47.8%), neutropenia - 3 (4.5%), leukopenia - 5 (7.5%), stomatitis - 5 (7.5%) and alopecia - 12 (17.9%). Hormone therapy was performed in patients after chemotherapy. Tamoxifen was used in 62 (92.5%) patients with recurrent breast cancer, sustanon was used in 4 (6.0%) patients, and oophorectomy was performed in one patient (1.5%). At the same time, the greatest number of side effects were associated with castration syndrome - 29.8%: hot flashes were observed in 18 (26.8%) patients, alopecia - in 2 (3.0%). Gastrointestinal disorders accounted for 13.4%: diarrhea in one patient (1.5%), vomiting also accounted for 1.5% and nausea was observed in 7 (10.4%) patients. Headaches, increased blood pressure amounted to a total of 8.0%. In the combined treatment of breast cancer recurrence, a sufficiently high level of local control was provided. The local cure rate was 72.6% ± 6.7%. Relapse-free survival with combined treatment turned out to be - 1 year without relapses lived 64.3 ± 5.8%, 3 years - 31.3 ± 5.6%, more than 5 years - 28.4 ± 5.5%. Among patients with recurrent breast cancer who received combined treatment, overall survival was: one-year 79.1 ± 4.9%, three-year - 59.9 ± 5.9%, five-year - 52.8 ± 6.7%. Local treatment was performed in 30 (16.5%) patients with loco-regional recurrences of breast cancer. At the same time, in some cases, surgical exposure was performed with or without radiation therapy, in others, only radiation treatment. Only surgical treatment was used in 3 (10.0%) patients with single recurrences of breast cancer, which were localized on the chest wall. The operative method was performed in the volume of excisional biopsy. The presence of concomitant diseases did not allow for systemic treatment and was also a contraindication for radiotherapy, and deep menopause, a long relapse-free period (more than 3 years) after treatment of the primary tumor, a single recurrent node and the volume of surgical intervention were regarded as favorable factors that allow limiting by this treatment. Complications were not observed. Surgical treatment followed by radiation therapy was performed in 14 (46.6%) patients with recurrent breast cancer. If the recurrence was localized in the mammary gland, a radical mastectomy according to Patey was performed, in other cases, an excisional biopsy was performed. There were no complications. At the second stage, the patients underwent radiation therapy, and if, in case of recurrence in the mammary gland, radiation therapy was used according to a radical program with a total focal dose of 44 Gy and a single dose of 2 Gy, then for other localizations, the total dose varied within 30-44 Gy, and a single dose - within 2 - 3 Gy. Complications in the form of radiation epidermitis were observed in 5 (16.7%) patients. Only radiation therapy was used in 13 (43.4%) patients with recurrent breast cancer in the localization of the latter on the chest wall and in the regional lymph nodes. The multiplicity of recurrent nodes was a contraindication for surgical treatment, and the presence of concomitant diseases or the patient's refusal were contraindications for systemic therapy. In case of local relapses, a dose of 40 Gy to 50 Gy was administered to the same half of the chest and the area of regional metastasis. Intact zones of regional lymphatic outflow, exposed to radiation at the stage of treatment of the primary tumor, were not re-irradiated. In case of isolated regional relapses, the entire supraclavicular-axillary zone of the same name was irradiated up to 40-50

Gy. Radiation epidermitis was observed in 3 patients (10%). Relapse-free survival with local treatment was: 61.5 + 8.8% lived for 1 year without recurrence, 28.1 + 8.2% - for 3 years, 25.6 + 7.9% - only for more than 5 years. In general, 73.3 + 8.1% survived 1 year, 51.0 + 9.1% survived 3 years, 43.7 + 9.1% survived more than 5 years. Only systemic treatment was carried out in 55 (30.2 %) of patients with multiple recurrent nodes. Monotherapy (doxorubicin, taxotere) was performed in 9.7% of patients in this group. It should be noted that often, when one or another chemotherapy regimen was ineffective, another line of chemotherapy drugs was used. With a systemic approach to treatment, 2 and 3 courses of chemotherapy were rarely performed (2.4% and 9.8%, respectively), more often due to pronounced and intractable side effects and exacerbation of chronic concomitant diseases. In the same cases, they were limited to 4 and 5 courses, which were carried out in 14.6% and 24.4%, respectively. Most often, 6 courses of chemotherapy were performed - in 34.2%, and when a pronounced antitumor effect was achieved, further courses were not performed. More than 6 courses were performed in 14.6% of patients with the progression of the process and with a fairly good tolerability of the drugs. At the second stage, the patients underwent hormone therapy. In 3 cases, oophorectomy was performed, in the remaining 29 cases, tamoxifen was used, which was used until the disease progressed. Duration of application ranged from 4 to 60 months. In this group of patients with recurrence of breast cancer in 14 (25.5%) patients, only hormone therapy with tamoxifen was used as treatment. This method was used in the presence of contraindications or refusal, the patient from other types of treatment, as well as with favorable prognostic factors (long relapse-free interval, deep menopause). With this therapeutic approach, the lowest frequency of local cure was noted - 37.3 + 6.2%. With systemic treatment, relapse-free survival turned out to be the lowest - 41.2 + 6.6% survived 1 year without relapses, 23.4 + 5.7% - 3 years, only 21.2 + 5.5% of patients survived more than 5 years. The overall survival rate was as follows: 65.4 + 6.4% survived 1 year, 40.6 + 6.7% survived 3 years, 31.8 + 6.5% of patients survived more than 5 years. The success of the treatment of patients with recurrent breast cancer is sometimes determined by the accuracy of diagnosis of the prevalence of the tumor process, and was complicated by the nature and characteristics of the existing functional disorders of the main life support systems of the body and concomitant diseases. Strict adherence to the tactics of a comprehensive examination of radically treated patients for breast cancer is a successful guarantee of timely diagnosis of relapses. The totality of data during the comprehensive examination made it possible to come to a fairly definite conclusion, and the negative results of one of the methods could not be the basis for excluding the tumor and required the use of additional methods. Based on the study of the immediate and long-term results of the treatment of recurrent breast cancer, it was found that and combined approaches that provide for adequate local treatment of a recurrent focus and the use of systemic methods of treatment have an undeniable advantage in terms of overall (64.0% and 52.8%, respectively) and relapse-free survival of patients (42.8% and 28.4%, respectively), compared with only a local or only systemic approach (43.7% and 31.8% - general and 25.6% and 21.2% - relapse-free, respectively). Therefore, when choosing treatment tactics for breast cancer recurrence, it is necessary to focus on an integrated approach, which can improve the quality of life of the patient, as well as increase her life expectancy.

CONCLUSIONS

The rate of recurrence increases in direct proportion to the prevalence of the primary tumor process: with T₁, the average time for the onset of relapse was 38.8 + 4.6 months, with T₂ - 30.1 + 3.9 months, with T₃ - 19.5 + 3.4 months and at T₄ 16.9 + 2.2 months. The average period of recurrence was shorter in the presence of metastases in regional lymph nodes and amounted to 26.5 + 4.4 months versus 41.6 + 5.8 months. - without them (p<0.05). In low-differentiated forms of breast cancer, the average period of recurrence is significantly less than 23.4 + 2.7 months than in moderately and highly differentiated forms: 31.3 + 3.2 and 41.5 + 3.6 months, respectively (p<0.05). In young women with preserved menstrual function, the average period of recurrence is significantly shorter than in

menopausal women - 17.3%±4.3 months. and 34.8%±5.4 months. respectively ($p<0.01$), therefore, they need to conduct a follow-up examination more often after the primary treatment of breast cancer with the rational use of diagnostic methods. This will allow timely detection of recurrence and ensure the implementation of a full-fledged complex or combined treatment, which can significantly improve the quality of life and indicators of overall and relapse-free survival of patients. Complex and combined methods of treatment of breast cancer relapses have an undeniable advantage in terms of overall (64.0%±8.9% and 52.8%±6.7%, respectively) and relapse-free 5-year survival of patients (42.8%±9.0% and 28.4%±5.5%, respectively), compared with local or systemic methods (43.7%±9.1% and 31.8%±6.5% - total and 25.6%±7.9% and 21.2%±5.5% - relapse-free, respectively) ($p<0.05$).

1. X Feruza Current concepts of breast cancer risk factors International journal of philosophical studies and social sciences 1 (3), 57-66,2021
2. KF Sharofovna, MU Sunnatovich, JN MODERN APPROACH TO BREAST CANCER SCREENING Ablokulovich European Journal of Life Safety and Stability (2660-9630) 7, 148-154,2021
3. MG Khasanovna, KF Sharofovna Features Computer-Dependence in Adolescents European Multidisciplinary Journal of Modern Science 4, 239-243,2022
4. KF Sharofovna MASTOPATHY AND BREAST CANCER PREVENTION AS AN INTERDISCIPLINARY ISSUE ИЖТИМОЙ ФАНЛАРДА ИННОВАЦИЯ ОНЛАЙН ИЛМИЙ ЖУРНАЛИ, 118-126,2022
5. ФШ Халикова СРАВНИТЕЛЬНАЯ ОЦЕНКА ХИРУРГИЧЕСКОГО ЛЕЧЕНИЯ РАКА ЖЕЛУДКА ОСЛОЖНЕННОГО КРОВОТЕЧЕНИЕМ Барқарорлик ва Етакчи Тадқиқотлар онлайн илмий журналы 1 (5), 181-188,2021
6. ЖР Нуров, ФШ Халикова LONG-TERM RESULTS OF SURGICAL TREATMENT PATIENTS WITH STOMACH CANCER Вестник науки и образования, 85-90,2020
7. ХН Абдуллаев, ЖР Нуров, ФШ Халикова, УС Мамедов Непосредственные результаты хирургического лечения больных раком желудка Проблемы биологии и медицины, 115,2019
8. UmidSunnatovich MAMEDOV, FSh KHALIKOVA Influence of Changes in the Intestinal Microflora after Gastrectomy and Correction Methods J Annals of the Romanian Society for Cell Biology, 1922-1926,2021
9. KhF Sh Advantages of Magnetic Resonance Computer Tomography in the Diagnosis of Thyroid Cancer Pindus Journal of Culture, Literature, and ELT 9, 80-84,2021
10. AN Narzulloyevich, MG Fazliddinovna, KhF Sharopovna Comparison of the results of modern methods of treatment of elderly women with breast cancer Eurasian Medical Research Periodical 3, 9-15,2021
11. Мухидова Г. Х.Феномен «компьютерной зависимости: особенности интернет-зависимости у подростков». Eurasian journal of medical and natural sciences, 2021.1(2), 22–26.
12. Мухидова Гулмира Хасановна. Comparative Characteristics of morphometric parameters of physical development and anthropo extremities of healthy and computer.Research.Jet Journal of Analysis and Inventions- RJA,Volume 2, Issue 9 Sep., 2021 14- 17pg
13. Мухидова Гулмира Хасановна. Морфометрические особенности параметров физического развития и антропометрических параметров верхней конечности 13 летних компьютерно-зависимых подростков мальчиков. Problems of biology and medicine (89) 2016г. стр.52-56.

14. Мухидова Гулмира Хасановна. Сравнительная характеристика компьютерно-зависимых компьютерно-независимых подростков по антропометрическим показателям. Тиббиётда янги кун 5(37)2021 й.169-171 бет
15. Mukhidova Gulmira Khasanovna. Features of Computer Dependence Comparative Characteristics of Computer-Dependent and Computer-Independent Adolescents by Anthropometric Indicators International Journal of Innovative Analyses and Emerging Technology| ISSN 2792-4025 (online), Published under Volume: 1 Issue: 4 in September-2021 <https://creativecommons.org/licenses/by/4.0/> 213-217
16. Мухидова Гулмира Хасановна. Сравнительная характеристика морфометрических параметров физического развития и антропометрических данных верхних конечностей здоровых и компьютерно-зависимых детей. “Современные направления в науке и технологии” 2016г.стр 408-411.
17. Мухидова Г.Х. “Zamonaviy ta’lim: muammo va yechimlari” Особенности антропометрических параметров компьютерно-зависимых подростков мальчиков. 2021г стр 49-50.
18. Мухидова Г.Х. “Zamonaviy ta’lim: muammo va yechimlari”.Морфофизиологические особенности и степень интернет-зависимости у подростков. 2021г стр 45-46.
19. Mukhidova G.X., Sanoev B.A. International Journal of Discoveries and Innovations in Applied Sciences|e-ISSN: 2792-3983|www.openaccessjournals.eu/ Published under Volume: 2 Issue: 3 in March-2022 Copyright (c) 2022 Author (s). Causes and Occurrence of Uterine Endometrial Polyps in Women in Bukhara Region 2022г.стр 42-45.