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OPPORTUNITIES FOR ORGAN-SAVING SURGERIES IN THE COMPLEX TREATMENT OF LOWER-AMPULAR RECTAL CANCER

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OPPORTUNITIES FOR ORGAN-SAVING SURGERIES IN THE COMPLEX TREATMENT OF LOWER-AMPULAR RECTAL CANCER

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ABSTRACT

Backgrounds. Colorectal cancer (CRC) incidence has a tendency to increase in recent decades in many countries of the world. The present research explores the data on indications for organ-preserving operations in the CRC and analyzes new criteria for their implementation. **Materials and research methods.** A retrospective analysis of the clinical data of 120 patients with colorectal cancer (CRC) with a T3-4N0-1M0 stage of the disease was carried out, who were observed in the Oncoproctology Department of RSSPMCO and the Ministry of Health Care of Republic of Uzbekistan in the period from 2005 to 2015. Patients were divided into the main and control clinical groups. The main group included 60 patients with RC who underwent various types of operations during complex treatment: abdominal-anal resection of the rectum (AARR), anterior resection of the rectum (ARR), Hartmann's operation. The control group included 60 patients with RC who underwent abdominal-perineal extirpation of the rectum (APER).

Results and discussion. The results of organ-preserving operations in the complex treatment of CRC were observed during three and five years. Cases of relapses and metastases were analyzed, and the survival of patients over a three- and five-year period was evaluated, depending on prognostic factors. During the three-year observation, local relapses in the main group occurred in 10 (16.6%) patients with RC and in the control group in 13 (21.7%) patients. The average relapse rate was $11,8 \pm 2,4$ months. **Conclusion.** A new method has been developed for the complex treatment of patients with CRC, including preoperative high-dose hypoxiradiotherapy, followed by organ-conserving operations. Besides a new approach has been developed for the complex treatment of patients with CRC, including preoperative endolymphatic polychemotherapy and regional lymphatic polychemotherapy, as well as in combination with hypoxiradiotherapy.

Key words: colorectal cancer, radiation therapy, ampullar colorectal cancer, perineal extirpation of the rectum.

Introduction.

The main and most effective method in the treatment of CRC is the surgical method, in compliance with the principles of oncological radicalism. However, the use of only the surgical method of treating CRC demonstrates low efficiency - over the past 20-25 years, 5-year survival rates, which average 52%, have remained stably low. In this case, the cause of death of approximately 68% of patients is relapse of cancer after surgery, and the incidence of locoregional metastases ranges from 20-40% [3]. These failures determine the feasibility of finding ways to increase an acceptable and effective method of treatment through the use of combined and complex treatment methods for CRC.

Recent decades have been characterized by the search for optimal regimens for combined and complex treatment of CRC by combining the surgical method with radiotherapy or chemotherapy in order to improve the treatment outcomes of a severe category of patients with a locally advanced process and the presence of metastases [4].

In modern clinical oncology, the search for the most effective methods for combining surgical intervention with various options for radiation therapy (preoperative, intra- or postoperative), as well as large-fraction ones [5]. At the same time, to date, there are no clear indications on the timing, doses and methods of exposure to radiation therapy in PKK, which indicates the need to find ways to improve and increase the effectiveness of this method of exposure [6].

The practical significance of the research results. Developed indications for organ-preserving surgical interventions for lower ampullar colorectal cancer, the most effective variants of chemoradiation methods have been proposed in the practical health care system of Uzbekistan.

The developed variants of the schemes and methods of combined and complex therapy, improvement of the surgical technique, methods of correction and prevention of complications help to reduce the incidence of early postoperative complications, mortality rate, as well as the occurrence of relapses and metastases,

which will increase the effectiveness of treatment, improve the quality of life of patients and reduce terms of their rehabilitation.

Based on the studies, the basic scientific provisions that are made are substantiated and formulated:

1. An analysis of the dependence of the number of postoperative complications in patients with colorectal cancer associated with performing surgical intervention showed that after organ-sparing surgeries, complications were observed in 14 (11.2%) patients, and after performing peritoneal perineal extirpation of the rectum (PPER) - in 14 (9.5%) patients. Analysis of postoperative complications of a general nature showed that their number did not depend on the type of surgical intervention.

2. On the example of 120 patients with rectal cancer with T3-4N0-1M0 stages of the disease, the possibility of performing organ-saving operations in this category of patients is shown. The presence of severe concomitant pathology along with the individual characteristics of tumor growth may serve as a contraindication to performing such operations.

3. New methods have been developed for the complex treatment of patients with colorectal cancer, including various schemes of preoperative high-dose radiation therapy, as well as methods of preoperative lymphatic polychemotherapy with subsequent organ-preserving operations.

4. The five-year survival rate for patients with colorectal cancer after complex treatment with organ-preserving surgeries was 75.2%, and in patients in the control group after complex treatment with PPER, 74.8%. Moreover, in the group of patients with organ-sparing surgeries after carrying out the methods of lymphatic polychemotherapy, this indicator amounted to 76.1%, and after various schemes of high-dose radiation therapy - 73.0%.

5. Organ-saving operations in the complex treatment of patients with rectal cancer with T3-4N0-1M0 stages of the disease significantly increase the quality of life of this category of patients, their social and labor rehabilitation, without compromising overall and relapse-free survival rates, which makes it possible to recommend the use of these techniques in complex treatment of this category of patients.

Diagnosis and treatment of locally advanced colorectal cancer. The five-year observation of patients with CRC in the T1N0M0 stage after surgical treatment is 90%; T2N0M0 after combined treatment - 70-80%; T3N0M0 after combined treatment - 60-65%, and after only surgical treatment 50-55%. T1-3N1-3M0 after combined treatment is 50-55%, and after only surgical treatment - 25-30%. In the T4N0-1M0 stage, 10-15% [8].

The situation when the neoplasm has exceeded not only the intestinal wall, but also the periintestinal tissue and has spread to nearby organs, or to the pelvic peritoneum, perivesical tissue, etc. commonly called locally distributed RC. [9] More broadly, the concept of locally distributed RC may include the following definition: an immobile or limitedly mobile tumor, circularly covering all the walls of the intestine, 5 cm long, narrowing the lumen of the intestine with the

involvement of neighboring organs and tissues and possible formation of fistulas or purulent cavities, and not having distant metastases [10].

The most adverse forms are mucous adenocarcinoma, cricoid-cell, undifferentiated cancer, and unclassified tumors. With a relatively small damage to the intestinal mucosa, they metastasize faster and more often spread not only to the entire intestinal wall, but also to surrounding tissues and organs. PKK can germinate in any adjacent organs or tissues. The bladder, small intestine, pelvic bones, ovaries, uterus, posterior wall of the vagina, prostate and seminal vesicles are most commonly affected. However, such germination is not always accompanied by distant metastasis, therefore, in such cases, it is advisable to conduct combined resections.

Local tumor growth and lymphogenous metastasis in RC are interrelated, but not always parallel. So, 15% of tumors limited by the muscle layer of the intestinal wall are accompanied by lymphogenous metastasis. When germinating in all layers of the intestinal wall, the lymph nodes are affected in more than 50% of cases. At the same time, even when the tumor invades the neighboring organs (locally advanced forms of cancer), lymphogenous metastasis is often (30%) absent.

According to many authors, 70-80% of patients with RC enter clinics with stage III-IV disease. Among the reasons for the late diagnosis of RC, it should be noted the absence of a mandatory standard examination scheme for a patient who suspects this disease, the inadequate use of previously developed diagnostic methods, and the limited use of new examination methods [11].

The primary RC is characterized by the fact that the tumor remains localized for a long time and grows relatively slowly compared to other tumors of the digestive tract. Localized and slow growth is also characteristic of metastases to the lymph nodes. Given this biological feature of RC, it was suggested that by increasing the number of lymphadenectomy, a reduction in the number of relapses can be achieved. At the same time, according to many researchers, the average five-year survival of patients, even when the operation is expanded to total pelvioabdominal lymphadenectomy, ranges from 45 to 60%. [12]

In this regard, increasing the effectiveness of treatment for RC, today remains an urgent problem of modern oncology. In recent decades, there has been a tendency to expand indications for organ-preserving operations in the RC. Many authors note that even with a pronounced spread of the cancer process, distant metastases may be absent, and it is possible to perform extended surgical interventions. [13] At the same time, it is necessary to formulate clear criteria for their implementation on the basis of a comparative analysis of the long-term results of treatment, the frequency of local regional relapses; the introduction of combined and comprehensive treatment programs that increase the flexibility of surgical interventions. [14]

Modern directions of organ-preserving surgical treatment of colorectal cancer. Modern methods of surgery for colorectal cancer are numerous. To choose one of them is directly dependent on the location of the tumor, its type of growth, degree of spread, its anatomical features, the patient's condition and the surgeon's

qualifications. When choosing surgical tactics in patients with colorectal cancer with sprouting into neighboring organs, one should be guided not only by such criteria as the size of the tumor, its location, growth form and histological structure, which always determine the technical capabilities of radical surgery, but such the most important prognostic factor, as the depth of tumor invasion. [15] An operation can be considered radical only if, along with a sufficiently wide resection of the area of the intestine affected by the tumor, the zone of possible regional metastasis is also removed.

The main and most effective method of treating RC is the surgical method, in compliance with the principles of oncological radicalism. However, the use of only the surgical method of treating RC demonstrates low efficiency - for 20–25 years, 5-year survival rates after radical surgeries remain at 46–62%, which is an average of 52%. Many authors attribute the main causes of failures in the surgical method of treatment to the occurrence of relapses and distant metastases that occur at different times after surgery. The cause of death in approximately 68% of patients is cancer recurrence after surgery, and the incidence of locoregional metastases ranges from 20-40%. [16] These failures determine the feasibility of finding ways to increase an acceptable and effective method of treatment through the use of combined and complex treatment methods for RC.

Among the many factors that determine the nature and extent of surgical interventions, and first of all organ-preserving ones, the fundamental role belongs to the degree of local spread of the tumor process and the level of tumor localization in the rectum. In RPK, typical operations depending on the height of the primary tumor are: anterior resection, abdominal-anal resection of the rectum with sigmoid reduction, obstructive resection (Hartmann's surgery) and abdominal-perineal extirpation (BPE) of the rectum [17]

Common forms of RC are often the main reason for abandoning active surgical tactics. Often, patients in this group perform symptomatic palliative surgery, in which there are a large number of postoperative complications and high rates of postoperative mortality. At the same time, the quality of life of these patients is significantly deteriorating, which is due to the increasing effect on their body of the not removed primary tumor and the progression of metastatic growth. The average life expectancy of these patients does not exceed 3–7 months. [18]

The main argument of opponents of superradical interventions is the high technical complexity and invasiveness of the latter. However, many surgeons do not agree with this judgment, since long-term world practice of performing combined and advanced operations not only allows us to hope for good long-term results, but also opens up great prospects for improving the quality of life of patients by performing simultaneous or delayed plastic surgeries. [19]

The current trend in locally advanced RC can be attributed to the tendency to perform saving interventions in the form of trans-abdominal resection and abdominal-anal resection of the rectum, naturally, in the absence of oncological contraindications. The postoperative mortality in these interventions is not much higher than that in conventional operations - for example, 30-40% of patients

undergoing combined operations survive a 5-year period. One of the important contraindications for performing combined operations is the presence of concomitant diseases that cannot be corrected in the preoperative period, especially in elderly patients. [20]

Materials and research methods. A retrospective analysis of the clinical data of 120 patients with colorectal cancer (CRC) with a T3-4N0-1M0 stage of the disease was carried out, who were treated in the Oncoproctology Department of RSSPMCO and the Ministry of Health Care of Republic of Uzbekistan in the period from 2005 to 2015.

Patients were divided into the main and control clinical groups. The main group included 60 patients with RC who underwent various types of operations during complex treatment: abdominal-anal resection of the rectum (AARR), anterior resection of the rectum (ARR), Hartmann's operation. The control group included 60 patients with RC who underwent abdominal-perineal extirpation of the rectum (APER).

In this case, the main and control groups of patients with RC were additionally divided into 3 subgroups depending on the nature of chemo- and radiotherapy (Tables 1, 2). Thus, patients in 1 subgroups received surgical treatment with endolymphatic polychemotherapy (ELPCH) and regional lymphatic polychemotherapy (RLPCH) and hypoxiradiotherapy (HRT), in 2 subgroups received surgical treatment in combination with radiotherapy (RT), in 3 subgroups received surgical treatment in combined with ELPCH and RLPCH.

We did not include in the observation of patients with acute intestinal obstruction, requiring emergency surgery, with a generalization of the process in the abdominal organs, ascites, lymphostasis, the presence of distant metastases, as well as with severe concomitant diseases requiring specialized treatment.

Table 1

Distribution of patients with colorectal cancer depending on the type of treatment in the main group, n = 60

Sub-Group	Type of operation	Combination therapy	Number of patients	
			Abs.	%
1	PRR, Hartmann's operation	ELPCHT	21	35,0
2	PARR	ELPCHT	23	38,3
3		LT	16	26,7
Total:			60	100

Table 2

Distribution of patients with colorectal cancer depending on the type of treatment in the control group, n = 60

Subgroup	Type of operation	Combination therapy	Number of patients	
			Abs.	%
1	PPER	ELPCHT+RLPCHT+HRT	19	31,7
2		ELPCHT+RLPCHT	24	40,0
3		LT	17	28,3
Total:			60	100

A study of the distribution of patients by gender and age showed that in the main group of patients with RC there were 34 men (56.7%) and 26 women (43.3%), in the control group these figures were 36 (60%) and 24 (40 %) respectively. The average age of patients in the main group was 49.1 ± 0.8 years, in the control group - 48.9 ± 0.7 years.

Table 3

Distribution of patients with colorectal cancer by gender and age in the main group, n = 60

Age	Gender				Total	
	Men		Women		Abs.	%
	Abs.	%	Abs.	%		
18-45	11	18,4	11	18,3	22	36,7
46-60	14	23,3	7	11,7	21	35,0
61 and upper	9	15,0	8	13,3	17	28,3
Total:	34	56,7	26	43,3	60	100

Table 4

Distribution of patients with colorectal cancer by gender and age in the control group, n = 60

Age	Gender				Total	
	Men		Women		Abs.	%
	Abs.	%	Abs.	%		
18-45	18	30,0	9	15,0	27	45,0
46-60	11	18,3	8	13,3	19	31,6
60 and upper	7	11,7	7	11,7	14	23,4
Total:	36	60	24	40	60	100

A study of the anamnesis of patients with PKK showed that in 17 (14.2%) of them, the duration of the disease was up to 3 months, in 42 (35%) - up to 6 months, in 36 (30%) - up to 1 year, in 13 (10.8%) - up to 2 years and 12 (10.0%) - up to 3 years (Table 5).

Table 5**Description of anamnesis of patients with colorectal cancer, n = 120**

Anamnesis of disease	Patients groups				Total	
	Main		Control		Abs.	%
	Abs.	%	Abs.	%		
Up to 3 months	3	5,0	6	10,0	17	14,2
Up to 6 months	14	23,3	12	20,0	42	35,0
Up to 1 year	19	31,7	26	43,3	36	30,0
Up to 2 year	17	28,3	14	23,4	13	10,8
Up to 3 year	7	11,7	2	3,3	12	10,0
Total	60	100	60	100	120	100

This subjective indicator shows the presence of an erased RC clinic, as evidenced by a three- and six-month history in less than half of patients (44.1%).

When conducting a rectoscopic examination, the exact localization of the tumor process and its extent was established (Table 6). As follows from the table, in the patients examined by us, the distal location of the tumor was mainly determined. So, during proctoscopy in 58 (48.3%) patients with CRC, the tumor was limited to localization in the anal canal. In rectoscopy in 50 (41.7%) patients, the tumor process was determined at a distance of 5–9 cm from the anus and in 12 (10%) patients at a distance of 10 cm or more from the anus level.

Table 6**Localization of the tumor process in relation to its location from the anus, n = 120**

Tumor localization	Patients groups				Total	
	Main		Control		Abs.	%
	Abs.	%	Abs.	%		
In the anal canal (up to 3-4 cm)	28	46,7	30	50,0	58	48,3
At a distance of 5-9 cm from the anus	26	43,3	24	40,0	50	41,7
At a distance of 10cm from the anus	6	10,0	6	10,0	12	10,0
Total:	60	100	60	100	120	100

In evaluating of disease prevalence, the TNM system was used (8th edition, 2008) (Table 7). As it follows from the table, stage IIa of the disease occurred in 18 (30.9%) patients, IIb in 32 (19.1%) and stage IIIb in 70 (50.0%) patients.

Moreover, in 32 (26.7%) patients there was a local spread of the tumor process (T4N0-1M0).

Table 7

Distribution of patients with colorectal cancer according to the stages of the disease and the TNM system, n = 120

Stage	TNM	Patients groups				Total	
		Main		Control		Abs.	%
		Abs.	%	Abs.	%		
IIa	T ₃ N ₀ M ₀	10	16,7	8	13,3	18	15,0
IIb	T ₄ N ₀ M ₀	16	26,7	16	26,7	32	26,7
IIIb	T ₃ N ₁ M ₀	18	30,0	20	33,3	38	31,7
	T ₄ N ₁ M ₀	16	26,6	16	26,7	32	26,6
Total:		60	100	60	100	120	100

The study of the histological structure of tumors showed that adenocarcinoma was predominantly found in 106 (88.3%) patients. At the same time, moderately differentiated adenocarcinoma was found in 39 (32.5%) patients, low-differentiated adenocarcinoma in 31 (25.8%) and highly differentiated adenocarcinomas in 36 (30.0%) patients with RC. Cricoid cell adenocarcinoma was diagnosed in 5 (4.2%) patients. Other histological forms of tumors were found in 9 (7.5%) patients.

Table 8

Distribution of patients with colorectal cancer depending on the histological structure of the tumor, n = 120

Histological form		Patients groups				Total			
		Main		Control		Abs.		Abs.	
		Abs.	%	Abs.	%				
Adeno carcinoma	Highly differentiated	14	23,3	22	36,7	36	30,0	106	88,3
	Moderately differentiated	25	41,7	14	23,3				
	Low differentiated	15	25,0	16	26,7				
	Cricoid cell	1	1,7	4	6,7				
Other forms	Slimy cancer	1	1,7	2	3,3	3	2,5	14	11,7
	Squamous cell carcinoma	1	1,6	1	1,7				
	Undifferentiated cancer	3	5,0	1	1,6				
Total:		60	100	60	100	120	100	120	100

Endolymphatic and regional lymphatic application of chemotherapy drugs. Preoperative endolymphatic polychemotherapy (ELPCH) and regional lymphatic chemotherapy (RLPCH) were performed in 47 (39.2%) patients with CRC, of which 23 (19.2%) were patients in the main group and 24 (20.07%) were in the control group.

At the same time, 21 (17.5%) patients of the main group underwent ELPCHT and RLPT in combination with hypoxiradiotherapy (HRT); in the control group, this type of treatment was used in 19 (15.8%) patients. Other 23 (19.2%) patients of the main group and 24 (20.0%) patients of the control group received only ELPCH and RLPCH.

Thin polyethylene catheters (PE10) were used for cannulation of the lymphatic vessels (Fig. 1).

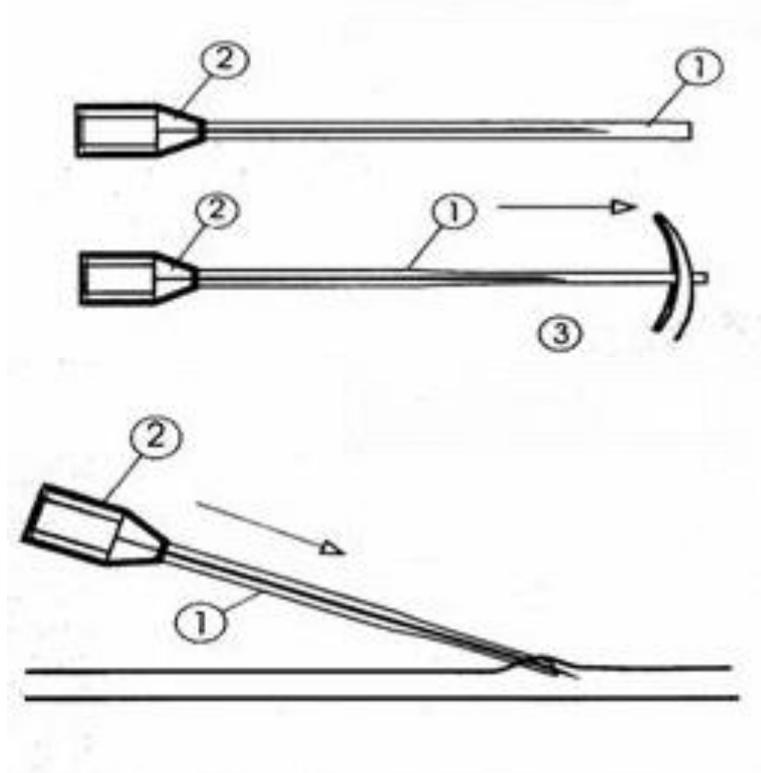


Fig. 1 Methods of catheterization of the peripheral lymphatic vessel of the lower limb. 1 - mandrin of an epidural catheter; 2 - polyethylene catheter PE 10; 3 - clamp.

Direct introduction of the cytostatic agent into the lymphatic channel provides a direct supply of the drug to the tumor and to metastases in the regional lymph nodes. This leads to an increase in the antitumor effect of chemotherapy with a decrease in the general and local toxicity of chemotherapy.

The duration of ELPCHT was 96 hours continuously:

- 1) methotrexate (Mtx) - 50 mg / m² for 24 hours in 24 hours, 1 day;
- 2) 5-fluorouracil (5-Fu) - 1000 mg / m² for 24 hours, 2, 3 days - 48 hours.

RLPCH (with the preliminary introduction of a cocktail of lymphostimulants, consisting of: Novocain - 0.25% - 4 ml, heparin - 2500 U, furosemide - 0.5 ml):

- 1) Mtx - 50 mg / m² 1 time, 4 days;
- 2) 5-Fu - 1000 mg / m² 1 time, 5.6 days.

The catheter is cut 2-3 mm longer than the mandrel. The protruding end of the catheter is fixed with a clamp and stretched until the catheter becomes thin (0.25-0.45 mm), while it should fit snugly against the mandrel. Then the catheter is cut 1-2 mm shorter than the mandrel.

Lymphatic catheterization for long-term administration of drugs was carried out as follows. The site of the procedure was chosen large interdigital gap on the rear foot. After treating the skin with 5% iodine solution and 96% alcohol, 1 ml of 1% methylene blue or 0.4% indigo carmine diluted in 0.25% 1.0 ml novocaine solution is introduced into the first interdigital space to stain the lymphatic vessel; retreating 5-6 cm upwards, a longitudinal skin incision of 2-3 cm was performed, a stained lymphatic vessel was found, it was isolated from adipose tissue and a dental spatula was placed under it. Previously, two ligatures were performed under the vessel, which were fixed with clamps directed to the proximal part of the wound.

To enlarge the vessel in diameter, it was pinched, pressing it above the incision with fingers. A cotton swab produced massage below the incision. After filling the vessel and increasing its size in diameter, a dental spatula was brought to the distal part of the wound. The lymphatic vessel became inactive. The vessel was punctured in its lower part by a specially prepared catheter, which was fixed with ligatures in two places above the entry into the lymphatic vessel. Then the mandrin was removed, the lymphatic vessel was checked for leaks by introducing a solution of novocaine through a catheter. 2-3 nodal sutures were applied to the skin. The free edge of the catheter was fixed with a band-aid to the skin. A needle was inserted into the free end and a chemotherapeutic system was connected. The drugs were injected with an electronic dispenser (ДЖИВ-1) at a rate of 1.0 ml / h. within 72 hours. In this case, Mtx was administered continuously - 50 mg / day x m² for 24 hours, on days 2 and 3 of 5-Fu - 1000 mg / day x m² for 48 hours. Then the lymphatic catheter was removed, and after treating the wound with 5% iodine, an aseptic dressing was applied.

After 6 days, a peripheral lymphatic vessel was catheterized on the back of the other foot, and the remaining half of the course dose of chemotherapy was slowly introduced into the catheter.

On the 4th day, RLPCHT was performed by injecting drugs into pararectal fiber, taking into account the localization of the tumor (Fig. 2).

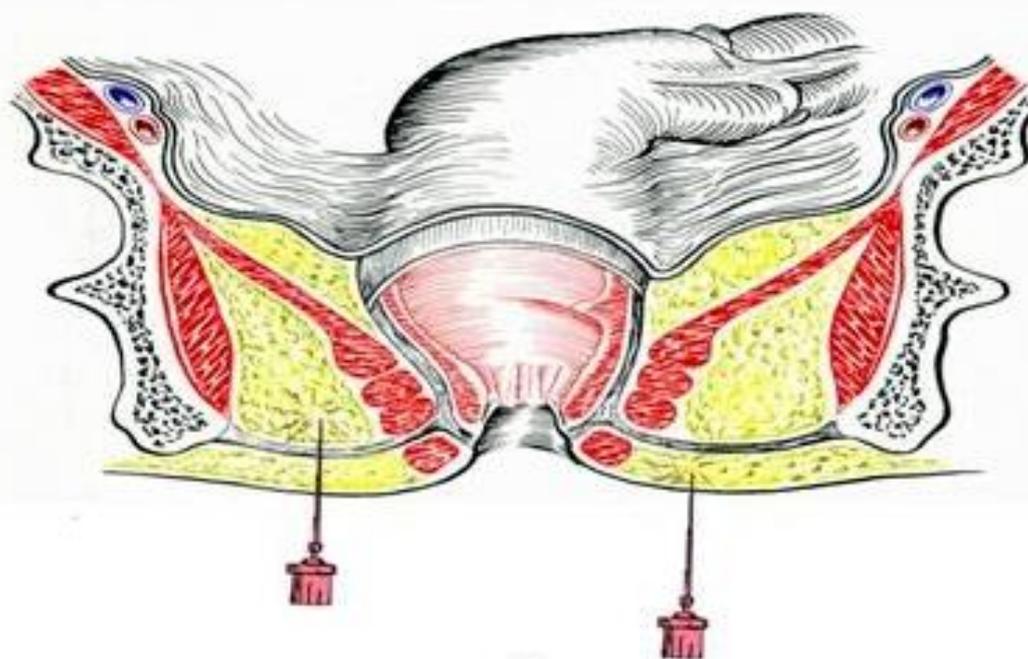


Fig. 2. Conducting regional lymphatic chemotherapy for colorectal cancer.

So, in case of a lesion of the anal canal by a tumor, the preparations were injected into the perianal tissue, and in case of the tumor of the middle and upper ampullar parts of the rectum, it was injected into the pararectal tissue closer to the tumor (i.e., to a depth of 8-10 cm from the skin).

To perform RLPCHT after thoroughly treating the perianal skin with 5% iodine solution and 76% alcohol, departing from the transition line 2 cm laterally, under the control of the finger inserted into the rectum, a needle was inserted into the pararectal tissue, leading its end towards the tumor.

For lymphostimulation, a cocktail of 0.25% 4.0 ml novocaine solution, 0.5 ml furosemide solution and 2500 IU heparin solution was administered. Then, without removing the needle, 3-5 minutes after complete lymphostimulation, the chemotherapy was administered through the same needle. Having removed the needle, a warming 40% alcohol compress was applied to this area for 5-6 hours. RLPCHT was performed on days 4 and 5, on day 4, Mtx was administered - 50 mg, then on day 5 5-Fu - 1000 mg of chemotherapy.

Along with the lymphotropic administration of water-soluble chemotherapy drugs, detralex was used 2 tablets 3 times a day during the course of chemotherapy in order to stimulate lymph drainage and lymphosorption in the lower extremities, to improve the penetration of chemotherapy drugs into the peripheral lymphatic channel and increase the concentration of these drugs in the lymph.

To prevent thrombosis in the lymphatic and venous bloodstream, a low molecular weight anticoagulant, fraxiparine, was administered at a dose of 0.3 ml subcutaneously 1 time per day during the administration of chemotherapy, under the control of PTI and VSK. In order to reduce the local cytotoxic effect by

additional dilution of the residual amount of chemotherapy drugs in the tissues and at the same time to re-stimulate their lymphosorption, a 0.5% novocaine solution up to 50 ml was injected subcutaneously at the site of the previous chemotherapy injection, immediately after removing the cuff from the hip. At the end of the procedure for the lymphotropic administration of water-soluble chemotherapy drugs to improve venous outflow and prevent venous thrombosis of the lower extremities, elastic bandaging of the lower extremities was performed after subcutaneous administration of novocaine.

Surgery was performed 7-14 days after the last lymphatic administration of drugs, during the period of the most pronounced decrease in the biological activity of the tumor due to PCHT.

Results and discussion. The results of organ-preserving operations in the complex treatment of CRC were observed during three and five years. Cases of relapses and metastases were analyzed, and the survival of patients over a three- and five-year period was evaluated, depending on prognostic factors.

During the three-year observation, local relapses in the main group occurred in 10 (16.6%) patients with RC and in the control group in 13 (21.7%) patients. Relapses developed at follow-up from 6 to 27 months. The average relapse rate was $11,8 \pm 2,4$ months.

Table 9

The frequency of relapse over a three-year period in patients with colorectal cancer, depending on the type of surgical treatment

Type of operation	The number of patients in groups	Patients groups			
		Main, n=60		Control, n=60	
		Abs.	%	Abs.	%
PRR with the anastomosis	main, n=12	1	8,3	–	–
PARR with the relegation proximal colon in the anal canal	main, n=14	2	14,2	–	–
PARR with the relegation sigma in anal canal	main, n=25	5	20,0	–	–
PARR with colostomy	main, n=6	1	16,6	–	–
Hartmann's operation	main, n=3	1	33,3	–	–
PPER with sigmostomy	control, n=60	–	–	13	21,7
Total:		10	16,6	13	21,7

The results of a univariate analysis showed that the frequency of relapse over a three-year period in patients with RR was higher after the PPER in 13 (21.7%) patients than in organ-preserving operations in 10 (16.6%) patients.

The frequency of relapse over a three-year period in patients with colorectal cancer, depending on the type of preoperative lymphatic chemotherapy:

An analysis of the dependence of the recurrence rate on the lymphatic chemotherapy regimen revealed that, in the ELPCHT + RLPCHT + HRT regimen, a smaller number of tumor relapses was observed compared to the regimen without HRT. In the main group of patients, in the first case, relapses were observed in 3 (14.2%) patients, while in the case of PCHT without HRT, in 4 (17.3%) patients.

The number of relapses in the case of a single GRT of 13 Gray turned out to be slightly lower compared with the ROD of 5 Gy to SOD 25 Gy. So, in the main group of patients with RC, with a 13 Gy GRT regimen, relapses were detected in 3 (14.2%) patients, and with a 5 Gy ROD regimen up to 25 Gy SOD, in 3 (18.7%) patients.

In stage IIa of the disease, the number of relapses was minimal and was observed in the main group in 1 (10.0%) patients with PKK, in stage IIb in 2 (12.5%), and in stage IIIb, the maximum number of relapses was found in 7 (20.6%) of patients.

The histological structure of the tumor also influenced the development of relapses in the distant postoperative period. The maximum number of tumor relapses in patients of the main group was found in undifferentiated form of cancer in 1 (33.3%) patients, in moderately differentiated adenocarcinoma in 5 (20.0%), and in low-grade adenocarcinoma in 3 (20.0%)) The least relapses were observed with highly differentiated adenocarcinoma - in 1 (7.1%) patients with CRC.

The macroscopic form of tumor growth also significantly affected the number of recurrences of RC. In the endophytic form of growth in the main group, we observed the highest number of relapses - in 4 (25.0%) patients, in the exophytic form - the smallest number of relapses - in 1 (7.1%), and in the mixed form of tumor growth, relapses were found in 5 (16.7%) patients.

Over a three-year period, tumor metastases to distant organs (liver and lungs) occurred in the main group in 5 (8.3%) patients with RC and in the control group in 4 (6.7%) patients. Metastases developed in the period from 6 to 18 months, which averaged $11,3 \pm 2,5$ months.

Moreover, the type of surgical intervention significantly influenced the development of metastases in the distant postoperative period, which is associated with various morbidity and volume of resected tissues of various surgical techniques. So, after Hartmann's operation, distant metastases occurred in 2 (66.7%) patients, after PARR with the relegation of the colon into the anal canal - in 1 (7.1%), after PPER with sigmoidostomy - in 4 (6.7%) and after PARR with the relegation of tyesygma into the anal canal - in 2 (8.0%) patients.

As a result of ELPCHT + RLPCHT in combination with HRT, distant metastases developed in 1 (4.8%) patients with major group RC, while metastases

were detected in 2 (8.7%) patients with the same chemotherapeutic effect, but without HRT.

At the same time, significant differences in the incidence of metastases over a three-year period in patients with colorectal cancer depending on the type of preoperative radiation therapy were not observed. So, after a single GDT at a dose of 13 Gy in the main group, metastases developed in 1 (4.8%) patients, and after an irradiation regimen of ROD of 5 Gy to SOD of 25 Gy - in 1 (6.2%) patients.

The incidence of metastases in the distant postoperative period also depended on the stage of the tumor process. So, in stage III b, metastases were detected in 4 (11.7%) patients of the main group, in stage II b - in 1 (6.2%) and metastases were not observed in stage II a.

The histological structure of the tumor also influenced the development of distant metastases. In the main group of patients with cricoid-cell form of cancer, metastases were found in 1 (100%) patients, with low differentiated adenocarcinoma - in 1 (6.7%), and with moderately differentiated adenocarcinoma - in 3 (12.0%). With highly differentiated adenocarcinoma, metastases were not observed.

In the endophytic form of tumor growth, metastases in the long-term postoperative period were determined in 2 (12.5%) patients of the main group, in the exophytic form of growth in 1 (7.1%), and in the mixed form of tumor growth in 3 (10.0 %) patients with RC.

An analysis of the three-year observation of patients with RC, depending on the type of surgical treatment performed, showed that the highest rate was observed after RC with anastomosis, where it was 91.7%. 3-year observation of patients after PARR with resection of the colon was 85.7%, after PARR with resection of sigma into the anal canal - 84.0%, after PPER with sigmoidostomy - 81.6%, after PARR with colostomy - 83.3%, and after Hartmann's operation - 66.7%.

The study of the three-year observation of patients with RC depending on the type of preoperative lymphatic chemotherapy showed that after the treatment regimen ELPCHT + RLPCHT + HRT, this indicator in the main group was 86.4%, and after ELPCHT + RLPCHT without HRT - 83.7%.

At the same time, the three-year observation rates after preoperative radiation therapy were almost identical and amounted to 83.8% after a single HRT at a dose of 13 Gy in the main group, and 80.6% after an ROD of 5 Gy to an SOD of 25 Gy.

The stage of the disease significantly affected the indicators of three-year observation of patients with RC. So, in the main group of patients, this indicator in stage IIa was 90.0%, in stage IIb - 87.5%, in stage IIIb - 79.4%.

The histological form of the tumor also significantly affected the three-year observation of patients with RC. In the main group of patients with cricoid adenocarcinoma and with undifferentiated cancer, mortality of patients for this period of time was not observed. With highly differentiated adenocarcinoma, this indicator was 92.8%, with moderately differentiated adenocarcinoma - 88.0%, with

low-grade adenocarcinoma - 80.0%. Three-year survival rates for low-grade cancer were 33.3%.

Three-year observation with the exophytic form of tumor growth in the main group of patients with RC was 92.8%, with the endophytic form - 75.0% and with the mixed form of tumor growth - 83.3%.

An analysis of the five-year survival of patients with PKK, depending on the type of surgical treatment performed, showed that the highest rate was observed after PRR with anastomosis, where it was 83.3%. the five-year survival rate of patients after PARR with relegation of the colon was 71.4%, after PPER with sigmoidostomy - 81.6%, after PARR with sigma relegation in the anal canal - 68.0%, after PARR with colostomy - 50.0%, and after Hartmann's operation - 66.7%.

A study of the five-year survival of patients with RC depending on the type of preoperative lymphatic chemotherapy showed that after the treatment regimen ELPCHT + RLPCHT + HRT, this indicator in the main group was 76.1%, and after ELPCHT + RLPCHT without HRT - 69.6%.

At the same time, the five-year observation rates in the main group of patients after preoperative radiation therapy were slightly lower and made to 76.2% after a single HDT at a dose of 13 Gy in the main group, and 62.5% after the radiation treatment regimen of 5 Gy to SOD 25 Gy.

The stage of the disease significantly affected the five-year observation of patients with RC. So, in the main group of patients, this indicator in stage IIa was 80.0%, in stage IIb - 81.2%, in stage IIIb - 61.8%.

In the main group of patients with undifferentiated cancer, with cricoid adenocarcinoma, with mucous cancer, with squamous cancer, five-year observation was not carried out. With highly differentiated adenocarcinoma, this indicator was 78.6%, - 80.0%, with moderately differentiated adenocarcinoma - 88.0%, with low-grade adenocarcinoma - 60.0%.

Five-year observation with an exophytic form of tumor growth in the main group of patients with RC was 78.6%, with an endophytic form - 56.2% and with a mixed form of tumor growth - 73.3%.

CONCLUSIONS

1. An analysis of postoperative complications of a general nature showed that their number did not depend on the type of surgical intervention. The rather large clinical material shows the possibility of performing organ-preserving operations in patients with lower ampullar cancer of the rectum.

2. A new method has been developed for the complex treatment of patients with colorectal cancer, including preoperative high-dose hypoxiradiotherapy according to schemes with a single exposure at a dose of 13 Gy (in 37 patients) and irradiation with medium fractions of 5 Gy up to SOD 25 Gy (in 36 patients), followed by organ-conserving operations. The five-year survival rate for patients with colorectal cancer after endolymphatic polychemotherapy and regional lymphatic chemotherapy with subsequent organ-preserving surgeries was 69.6%, with the addition of preoperative hypoxiradiotherapy to 76.1%. The five-year

survival rate after a single hypoxiradiotherapy at a dose of 13 Gy with subsequent organ-preserving surgeries was 76.1%, and after an irradiation regimen of ROD of 5 Gy to SOD of 25 Gy - 62.5%.

3. A new approach has been developed for the complex treatment of patients with colorectal cancer, including preoperative endolymphatic polychemotherapy and regional lymphatic polychemotherapy (in 47 patients), as well as in combination with hypoxiradiotherapy (in 40 patients), followed by organ-preserving operations.

4. An analysis of the five-year observation of patients with RC, depending on the type of surgical treatment, showed that the highest rate was observed after PRR with anastomosis, where it was 83.3%. the five-year observation rate of patients after PARR with relegation of the colon was 71.4%, after PPER with sigmoidostomy - 81.6%, after PARR with sigma relegation in the anal canal - 68.0%, after PARR with colostomy - 50.0%, and after Hartmann's operation - 66.7%. In patients of the control group, the five-year observation rate after performing PPER with sigmoidostomy was 68.3%.

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