



ROLE OF PREOPERATIVE RADIATION THERAPY IN COMBINED TREATMENT OF RESECTABLE RECTAL CANCER

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Article history:	Abstract:
Received: November 11 th 2023 Accepted: December 11 th 2023 Published: January 14 th 2024	Colorectal cancer is one of the most common cancers in the world. In the Russian Federation, about 40 thousand new cases of the disease are registered annually. Five-year survival rate for rectal cancer depends on the stage of the disease and ranges from 50% for stage I to 20% for stage IV. Currently, combined treatment with radiation therapy is the standard of care for resectable rectal cancer. Radiation therapy can reduce the size of the tumor, which facilitates surgery, and reduces the risk of local recurrence of the disease.

Keywords:

In recent decades, there has been a steady increase in the incidence of colorectal cancer throughout the world, which is taking leading positions in the structure of morbidity and mortality [Davydov M.I., Aksel E.M., 2010; Kaprin A.D. et al., 2016]. In the United States in 2016, 39,220 new cases of colorectal cancer were identified. From 50 to 80% of patients with rectal cancer are admitted to clinics in the late stages of the disease, which significantly worsens the prognosis and makes the success of treatment questionable [Ferlay J. et al., 2013]. Despite advances in the field of radiation and drug therapy, as well as advances in recent years in the field of molecular biology of cancer, the surgical method still remains the leading method in the treatment of this pathology. However, despite the abundance of modern surgical techniques, many fundamentally new designs of suturing devices and modern high-tech equipment of operating rooms, the improvement of the surgical method from an oncological point of view has to a certain extent reached its limit, as evidenced by the lack of significant improvements in long-term results of surgical treatment in recent decades [Pahlman L. et al., 2007; Peeters KC et al., 2007; Visser O. et al., 2007; Hansen MH et al., 2009; Elferink MA et al., 2010;]. At the same time, methods of combined treatment of RPC began to be developed, including preoperative large-fraction radiation therapy with SOD 25 Gy [Barsukov Yu.A., 1991; Knysh V.I., 1997; Pravosudov I.V. et al., 2012; Folkessen J. et al., 2005; Kapiteijn E. et al., 2001; Suwinski R. et al., 2007; Watanabe T. Et al., 2002], and postoperative radiation therapy according to a radical program (SD 60 Gy) [Brizel H., Tepperman B., 1984; Hoskins RB et al., 1985; Glimelius B. et al., 2003], as well as a combination of preoperative and postoperative radiation therapy, especially with metastatic lesions of regional lymph nodes [Barsukov Yu.A. et al., 2004; Babini L. et al., 1984; Hoskins RB et al., 1985;

Mohiuddin J. et al., 1982]. 4 Complicated cancer often precludes preoperative RT, highlighting the need for urgent surgical intervention. In this case, when metastases are detected in regional lymph nodes, one has to limit oneself to postoperative radiation therapy only. To enhance the effectiveness of preoperative RT, local microwave hyperthermia began to be used as a radiomodifier [Dudnichenko A.S. et al., 2000; Knysh V.I. et al., 1997; Nevolskikh A.A., 2000; Tamrazov R.I. et al., 2011; van der Zee J. et al. 2000;]. However, despite the reduction in relapse rates, this did not improve survival rates. This circumstance gave rise to a further search for ways to enhance the effectiveness of preoperative RT, which is especially important for cancer of the lower ampullary localization, and led to the creation of techniques using a combination of several radiation therapy modifiers with different mechanisms of action and points of application [Ichikawa D. et al., 1996; Ohno S. et al., 1997; Rau B. et al., 1998; Kang MK et al., 2011]. Since 2004, at the Russian Cancer Research Center named after. N.N. Blokhin developed a number of techniques using polyradiomodification (PRM), including the use of local microwave hyperthermia, Metronidazole (MZ) delivered endorectally to the tumor, and the fluoropyrimidine drug Capecitabine in radiosensitizing and therapeutic doses. However, to develop an individualized approach, it is necessary to develop a rational strategy that promotes the optimal choice of combined treatment method and the volume of surgical intervention to achieve the best oncological results. Oncological and functional adequacy of treatment follows from the preference of one or another volume of surgical intervention compared to other operations, depending on the combined treatment technique used, and consists in achieving, with minimal functional damage, a reduction not only in the frequency of locoregional cancer relapses, but also, if possible, distant



metastases. Modern diagnostic methods (transrectal ultrasound, MRI of the pelvic organs) make it possible to obtain information about the degree of local spread of the tumor and the condition of regional lymph nodes even before the start of treatment, which makes it possible to plan the latter in advance [Grishkov S.M. et al., 2013; Kotlyarov P.M. et al., 2012; Toropov V.Yu., 2004; Usova A.V. et al., 2012; Brown G., 2010; Russo S., Blackstock W., 2013].

THE PURPOSE OF THE DISSERTATION WORK:

The aim of the study is to examine the role of preoperative radiotherapy in the combined treatment of resectable rectal cancer.

MATERIALS AND METHODS. The master's thesis is based on the results of examination and treatment of 118 patients with resectable rectal cancer, who underwent surgical or combined treatment in the clinic of the Samarkand Branch of the Republican Scientific and Practical Medical Center and R in the period 2021-2024.

The results of all research methods used in clinical practice for the management of patients diagnosed with rectal cancer will be retrospectively analyzed. The main and control groups will be formed both retrospectively and prospectively, depending on the nature of the formulation of the specifically solved problems of the dissertation. Statistical processing of the received information will be carried out using standard statistical research procedures on computer equipment.

RESEARCH OBJECTIVES:

1. To optimize the method of combined treatment by increasing the dose of preoperative tumor irradiation and expanding radiation exposure to areas of regional metastasis.
2. Change the method and technique of surgical treatment through total mesorectumectomy, preservation of the pelvic autonomic nervous system, and expansion of indications for sphincter-preserving operations.
3. To evaluate the immediate results of combined treatment according to the criteria: radiation reactions, proliferative activity of the tumor, morphological changes in the tumor, postoperative complications.
4. To study the long-term results of treatment after organ-saving operations in terms of the frequency of local relapses and survival.
5. To evaluate the effectiveness of an improved treatment method in terms of local recurrence rates and three-year survival.

In this dissertation, in patients of the study group, surgical intervention in the amount of total mesorectumectomy was supplemented with

preoperative irradiation at a dose of 25 Gy. This method of combined treatment of patients with resectable rectal cancer has been used in our center since 1999. It combined modern principles of radiation therapy and modern methods of surgical treatment. The main differences between radiation therapy and previously used techniques are:

1. multifield irradiation, in contrast to the field rotation technique in patients in the control group.
2. higher, based on modern concepts, the total dose of radiation therapy.
3. preferential irradiation at a linear accelerator.
4. better topometric marking of radiation fields using computed tomography.
5. inclusion in the 95% isodose of not only the primary tumor and perirectal tissue, but also all areas of regional metastasis, i.e. increasing the volume of irradiation.

The main difference in the surgical intervention technique was the principle of "sheathing" - removal of the tumor and surrounding tissue within the existing anatomical layers in a sharp way under direct visual control. A mandatory aspect of the operation was the high ligation of the central vessels - the inferior mesenteric artery (at the base or below the origin of the left colon artery) and the vein (below the ligament of Treitz).

The immediate objectives of the study were to evaluate treatment results according to the following criteria: frequency of radiation reactions and postoperative complications, morphological changes in the tumor after irradiation, except

In addition, an assessment of the relapse rate and survival of patients compared with historical controls.

CONCLUSIONS: Intensive preoperative radiotherapy at a dose of 25 Gy (equivalent to 40 Gy with traditional fractionation) despite an increase in the number of general to 35% (grades 1-2 - 31.7%; grade 3 - 3.3%) and local to 13.3% (1-2 degrees - 10%; 3 degrees - 3.3%) of radiation reactions, was realized in all patients, in no case did it become a reason to transfer the operation abroad at an optimal time for it, and did not increase the number of postoperative complications. Radiation therapy changed the proliferative activity of tumor cells, significantly reducing the level of proliferation proteins (PCNA before treatment 59.2 ± 2.2 , after treatment 29.6 ± 2.1 , $p=0.0003$; cyclin A before treatment 23.7 ± 2.0 , after treatment 18.9 ± 1.5 , $p=0.03$).

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