

ORIGINAL ARTICLE

SURVIVAL OF PATIENTS WITH RECTAL CANCER

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ABSTRACT

The aim: To evaluate the early and late results of treatment of rectal cancer patients after special treatment methods with a view to identifying optimal method of treatment in correlation with the stage of the disease.

Materials and methods: The study is based on the results of observation of 779 patients with stage II, III and IV rectal cancer (RC) who were divided into groups according to the treatment (surgery, surgery + chemotherapy, chemotherapy, surgery + chemotherapy + radiation therapy, radiation therapy + surgery, radiation therapy).

Results: According to the results obtained, the overall survival of patients correlates with the stage of rectal cancer: we see the highest percentage of patients' survival in stage II and, accordingly, the lowest – in stage IV in each of the studied time intervals.

Conclusions: The use of combined and integrated treatment in patients with stages II and stage III and the use of chemotherapy in stage IV RC gives a higher rate of cumulative survival of patients at each of the studied intervals

KEY WORDS: rectal cancer, surgical treatment of rectal cancer, chemotherapy of rectal cancer

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INTRODUCTION

Rectal cancer is one of the most common malignancies: about 100,000 and 40,000 new cases are reported annually in Europe and the United States, respectively [1].

According to the data of the National Chancellery of Ukraine, the structure of malignant neoplasms (MN) among population of Ukraine (excluding non-melanoma skin cancer) RC 5.4% occur in women and 6.8% – in men. The morbidity among women with RC aged 55-74 is 6.1%, and among men – 7.2%, and among women over 75 years old – 7.3%

The mortality of the population of Ukraine with malignant neoplasms in men aged 55-74 is 6.2%, in men aged 75 and older – 9.1%. Among women aged 75 and older the mortality is 8.4% (2018 – refined information).

In 2019 according to the National Chancellery of Ukraine 23.7% and 19.7% of primary identified patients with RC stage III and stage IV were diagnosed. 2019 special treatment was introduced to 72.1% of patients. Mortality within a year was 25.4% [2].

Treatment for patients with advanced rectal cancer includes surgery, radiation and chemotherapy [3, 4].

The nature and extent of surgery depends on the location and spread of the tumour, complications and the general condition of the patient [5-7].

There is no definitive treatment and diagnosis standard for locally advanced rectal cancer, and sphincter-sparing surgery is not always possible. [8].

According to the NCCN Clinical Practice Guidelines in Oncology: there is no clear answer regarding the use of chemotherapy for the treatment of patients with stage II rectal cancer, as well as elderly patients [9- 12].

Patient survival is an objective indicator of the effectiveness of the therapy used.

Survival of RC patients correlates with the stage of the disease. There are many prognostic factors that affect the survival of patients: the presence of tumour cells at the edge of resection, lymphatic vascular invasion, microsatellite instability, perineural invasion, and so on [13, 14].

From the standpoint of the above, it is important to conduct further research aimed at developing new options for the treatment of patients with rectal cancer.

THE AIM

The purpose of the study is to evaluate the immediate and long-term results of treatment of patients with rectal cancer after special treatment in the CHPI «Precarpathian Clinical Oncology Center» in order to determine the effective treatment method of the stage of the disease.

MATERIALS AND METHODS

The basis of the study deals with the results of observation of 779 patients with rectal cancer in Communal Health Protection Institution «Precarpathian Clinical Oncology Center» from 2012 to 2018.

The direct and long-term results of treatment of rectal cancer were studied and evaluated.

All patients were divided according to the stage of the disease (TNM system): patients with stage II, stage III and stage IV rectal cancer. We analyzed the results obtained by comparing the investigated parameters within each of the

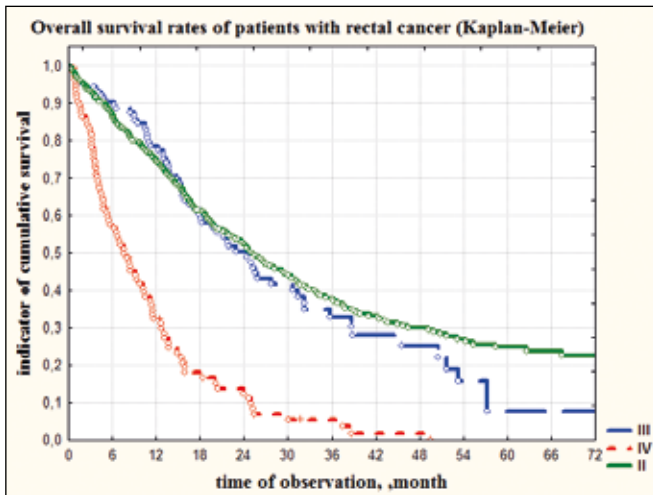


Fig. 1. Overall survival rates of patients with RC, taking into account the stage of the disease

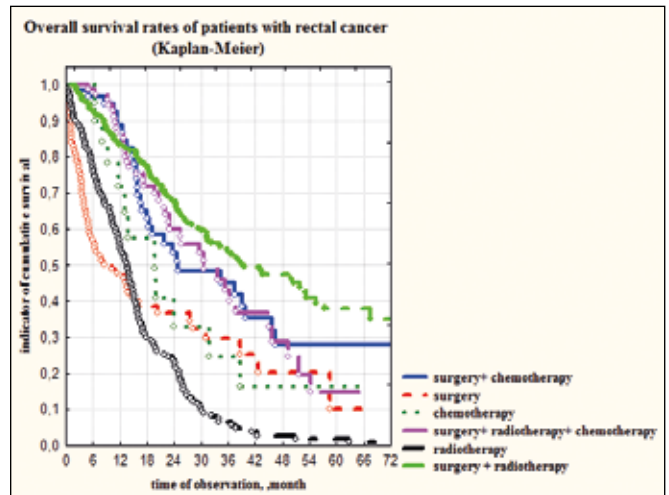


Fig. 2. Overall survival of patients with stage I-IV RC according to the treatment method

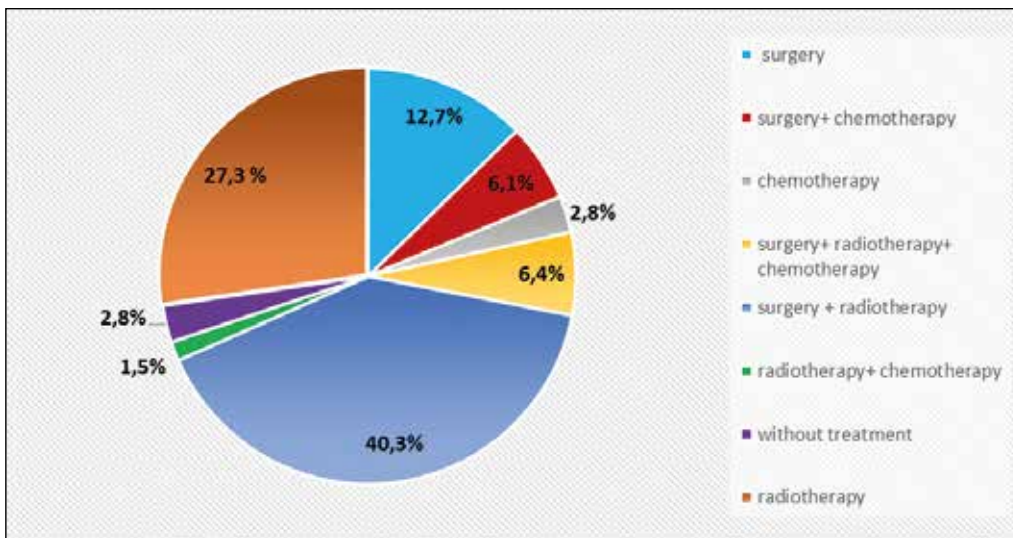


Fig. 3. Structure of treatment of stage II RC

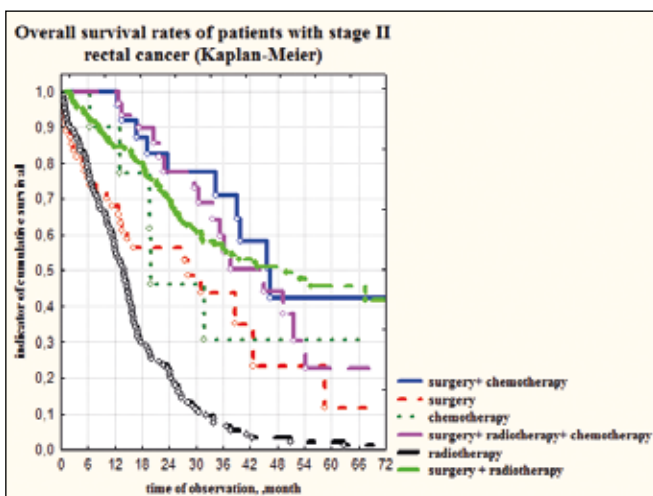


Fig. 4. Overall survival rates of patients with stage II RC, according to the treatment method

stages of rectal cancer and together for the total number of patients, determining their effect on their survival.

RESULTS

For the initial analysis of the effect of treating patients on the overall survival rates, we calculated the cumulative survival rates and the percentage of the overall survival of rectal cancer in patients, taking into account the stage of the disease, but without treatment received (Fig. 1)

Analyzing the results we see the highest percentage of survival in stage II and, accordingly, the lowest – in stage IV in each of the studied time intervals, starting with the 24th month of observation (Table I).

At the next stage of the study we analyzed what treatment methods were received by the patients. The treatment methods included the following: surgery, surgery + chemotherapy, chemotherapy, surgery + chemotherapy + radiation therapy, radiotherapy + surgery, radiotherapy (Table II).

The cumulative survival rate is determined for the total number of patients depending on the treatment method (Fig. 2).

According to the calculations $p = 0.00000$, which indicates the effect of the treatment method on the cumulative survival rate of patients for the total number of patients.

For the total number of patients under study, regardless of the rectal cancer stage, at each time intervals, we ob-

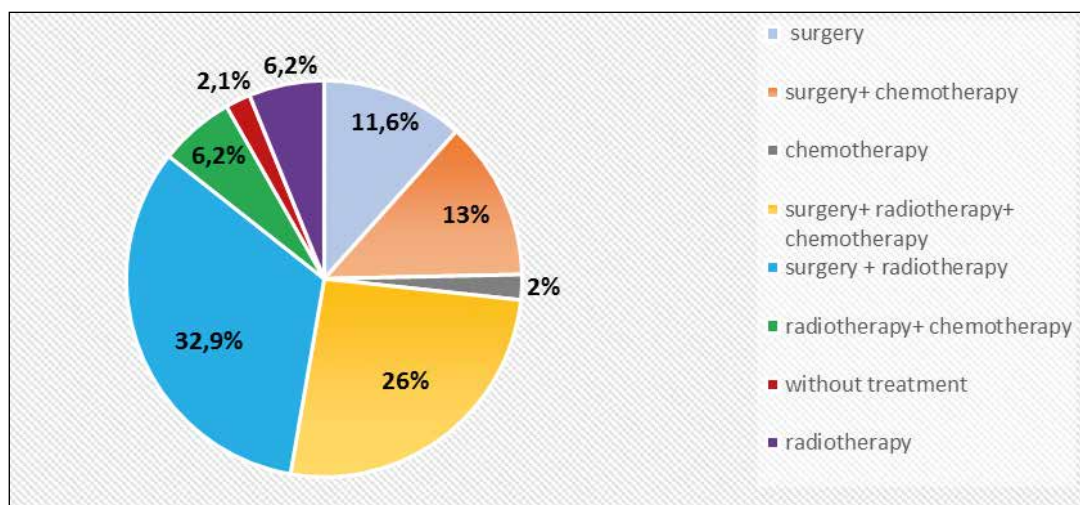


Fig. 5. Structure of treatment of stage III RC

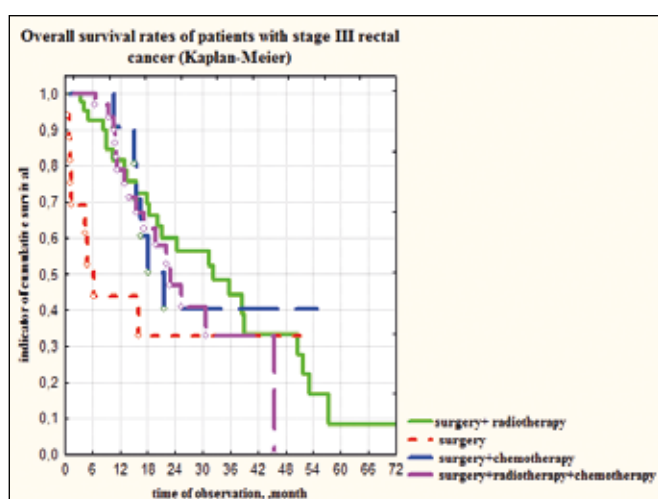


Fig. 6. Overall survival rates of patients with stage III RC, according to the treatment method

served a higher percentage of patients who survived with the combined and integrated treatment than patients, who received only surgery, radiotherapy or chemotherapy (Table III, Table IV).

In order to determine the best treatment method for patients with rectal cancer, we analyzed the overall survival rates separately for stage II, stage III and stage IV of the disease, taking into account methods of treatment of patients.

ANALYSIS OF THE CUMULATIVE SURVIVAL RATE OF PATIENTS WITH STAGE II RECTAL CANCER

There was 67.8% of the total number of patients (528 people) with stage II rectal cancer, 97.2% of patients received special treatment (513 patients). Surgical treatment was received by 67 patients (12.7%), surgery + chemotherapy – by 32 people (6.1%), chemotherapy – by 15 patients (2.8%), radiation therapy – by 144 patients (27.3%), surgery + chemotherapy + radiotherapy- (6.4%), surgery + radiotherapy – by 40.3% and chemotherapy + radiotherapy – by 1.5% of patients (8 people) (Fig. 3).

Analysis of the cumulative survival rate of patients depending on treatment method (Fig. 4).

According to the calculations $p = 0.00000$, which indicates the effect of treatment method on the cumulative survival rate of patients.

For patients with stage II rectal cancer, at each studied time intervals, starting with 24th month of observation,

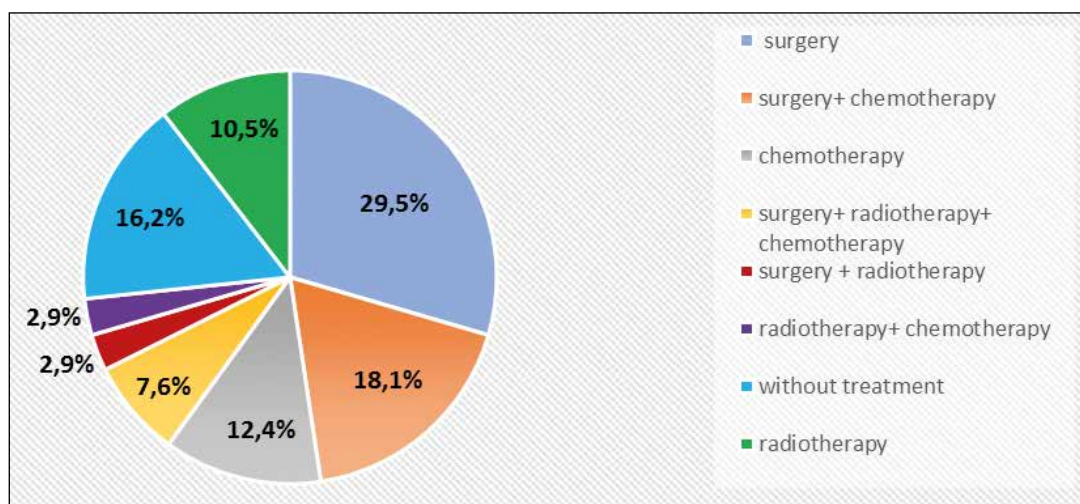


Fig. 7. Structure of treatment of stage IV RC

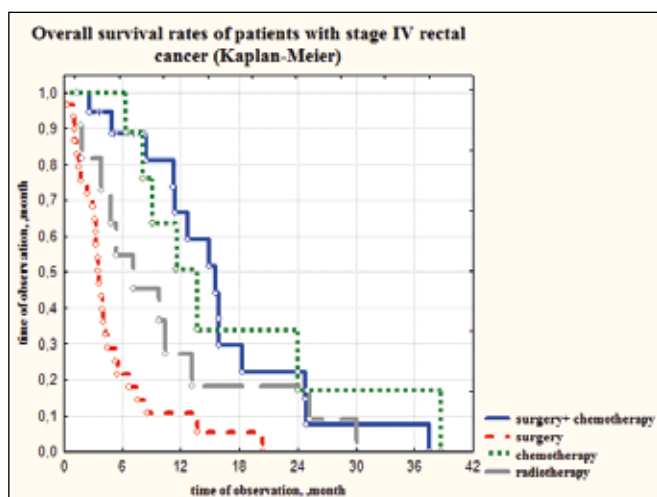


Fig. 8. Overall survival rates of patients with stage IV RC, according to the treatment method

we see a higher percentage of patients, who survived with a combined and integrated treatment than patients with surgery, radiotherapy or chemotherapy. Thus, 8.4%, 1.6% and 7.7% of patients with surgery, radiotherapy or chemotherapy survived on the 5th year of observation.. The smallest percentage of the survived patients is noted in the group with the use of radiotherapy as a treatment method only. Then, the same indicators in patients who received treatment are observed: surgery + radiation therapy, surgery + radiation therapy + CT and surgery + CT- 45.6%, 21.1% and 30.0% respectively (Table V, Table VI).

ANALYSIS OF THE CUMULATIVE SURVIVAL RATE OF PATIENTS WITH STAGE III RECTAL CANCER

There were 18.7% of patients (146 people) with stage III rectal cancer. 97.9% of patients have undergone special treatment (143 patients). Surgery was received by 17 patients (11.6%), surgery + chemotherapy – by 19 people (13%), chemotherapy – by 3 patients (2%), radiotherapy – by 9 patients (6.2%), surgery + chemotherapy + radiotherapy – by 38 patients (26%), surgical + radiotherapy – by 48 patients (32.9%) and chemotherapy + radiotherapy – by 6.2% of patients (9 people) (Fig. 5).

Analysis of the cumulative survival rate of patients depending on treatment method (Fig. 6).

According to the calculations $p = 0.0111$, which indicates the effect of treatment method on the cumulative survival rate of patients.

For patients with stage III RC we see a higher percentage of survival in the group of patients, who received surgery + radiotherapy at each of the studied time intervals, starting from the 24th month of observation. This is the only group of patients with stage III RC, where the survival was seen on the 5th year of observation.

The smallest percentage of patients survived is noted in the group of patients, who received surgery compared with combined and integrated therapy on the 6th, 12th, 24th and 36th months of observation.

Thus, the patients who survived on the 3rd year of observation received only surgery -14.1%, against 45.4% and 32.4% patients – with combined treatment (surgery + radiation therapy) and complex treatment (surgery + radiotherapy + chemotherapy) respectively. (Table VII).

Table I. Overall survival rates of patients with rectal cancer (%)

Time of observation, month	% of patients survived			Standard error		
	Stage II	Stage III	Stage IV	Stage II	Stage III	Stage IV
6	87.2	90.2	58.0	± 1.5	± 2.6	± 4.9
12	74.9	78.9	33.0	± 2.0	± 3.8	± 4.9
24	52.6	50.9	14.4	± 2.5	± 5.3	± 3.9
36	38.1	33.8	5.6	± 2.6	± 5.5	± 2.7
48	29.9	26.5	0.9	± 2.7	± 5.7	± 1.3
60	24.7	11.0		± 2.8	± 5.9	

Table II. General characteristics of the received treatment in patients

Treatment	Stage II	Stage III	Stage IV	Total
Surgery	67	17	31	115
Chemotherapy	15	3	13	31
Surgery+ Chemotherapy	32	19	19	70
Surgery+ Chemotherapy + Radiotherapy	34	38	8	80
Surgery+ Radiotherapy	213	48	3	264
Radiotherapy	144	9	11	164
Chemotherapy + Radiotherapy	8	9	3	20
Total	513	143	88	744

Table III. Overall survival (%) of patients with rectal cancer, depending on method of treatment

Time of observation, month	% of patients survived					
	Surgery	Radiotherapy	Chemotherapy	Surgery+ Chemotherapy	Surgery + Radiotherapy + Chemotherapy	Surgery + Chemotherapy
6	59.0	78.5	98.0	93.1	98.7	96.8
12	49.5	56.7	71.5	83.7	87.2	89.0
24	37.9	23.9	40.9	68.2	60.4	54.0
36	30.7	6.4	24.5	54.5	43.9	45.7
48	20.2	2.8	12.3	47.6	29,5	28.0
60	8.1	1.4	6.9	38.3	14.6	22.5

Table IV. Calculation of standard error

Time of observation, month	Standard error					
	Surgery	Radiotherapy	Chemotherapy	Surgery + Radiotherapy	Surgery + Radiotherapy + Chemotherapy	Surgery+ Chemotherapy
6	± 4.8	± 3.3	± 2.7	± 1.6	± 1.3	± 2.2
12	± 5.1	± 4.1	± 10.3	± 2.5	± 4.0	± 4.2
24	± 5.3	± 3.7	± 13.1	± 3.3	± 6.4	± 7.3
36	± 5.8	± 2.2	± 11.9	± 3.8	± 7.1	± 7.6
48	± 7.2	± 1.5	± 9.3	± 4.1	± 7.7	± 7.8
60	± 6.9	± 1.1	± 6.6	± 4.6	± 7.3	± 8.0

Table V. Overall survival (%) of patients with stage II rectal cancer depending on method of treatment

Time of observation, month	% of patients survived					
	Surgery	Radiotherapy	Chemotherapy	Surgery + Radiotherapy	Surgery + Radiotherapy + Chemotherapy	Surgery + Chemotherapy
6	76.9	79.9	96.2	93.5	98.5	98.2
12	68.8	57.6	86.0	84.9	96.8	96.3
24	55.5	22.8	43.7	70.6	74.9	74.7
36	43.3	7.4	24.3	57.2	58.0	66.2
48	22.5	3.2	13.6	50.8	42.6	39.3
60	8.4	1.6	7.7	45.6	21.1	30.0

Table VI. Calculation of standard error

Time of observation, month	Standard error					
	Surgery	Radiotherapy	Chemotherapy	Surgery + Radiotherapy	Surgery + Radiotherapy + Chemotherapy	Surgery + Chemotherapy
6	± 5.4	± 3.5	± 5.3	± 1.8	± 2.2	± 2.5
12	± 6.2	± 4.4	± 10.7	± 2.6	± 3.1	± 3.7
24	± 7.1	± 3.9	± 18.4	± 3.6	± 8.3	± 9.0
36	± 8.5	± 2.5	± 15.5	± 4.2	± 9.8	± 10.3
48	± 11.7	± 1.8	± 11.8	± 4.5	± 1.5	± 12.1
60	± 8.2	± 1.3	± 8.0	± 4.9	± 10.4	± 12.4

Table VII. Overall survival (%) of patients with stage III rectal cancer depending on method of treatment

Time of observation, month	% of patients survived				Standard error			
	surgery	surgery+ radiotherapy	surgery+ radiotherapy+ chemotherapy	surgery+ chemotherapy	surgery	surgery+ radiotherapy	surgery+ radiotherapy+ chemotherapy	surgery+ chemotherapy
6	53.3	93.1	98.6	96.9	± 12.8	± 3.8	± 1.9	± 4.3
12	44.4	82.2	79.5	88.8	± 13.5	± 6.2	± 7.2	± 8.7
24	25.0	60.2	48.1	40.5	± 14.6	± 8.4	± 10.4	± 15.2
36	14.1	45.4	32.4	27.8	± 11.6	± 9.1	± 11.7	± 14.9
48	7.0	32.9		15.6	± 7.6	± 9.5		± 12.3
60		9.9				± 7.1		

Table VIII. Overall survival (%) of patients with stage IV rectal cancer depending on method of treatment

Time of observation, month	% of patients survived				Standard error			
	surgery	radio-therapy	surgery+ chemotherapy	chemotherapy	surgery	radio-therapy	surgery+ chemotherapy	chemotherapy
6	21.6	54.5	88.6	95.2	± 7.8	± 15.0	± 7.6	± 6.6
12	5.4	27.3	68.1	50.4	± 4.8	± 13.4	± 11.9	± 16.7
24		13.6	22.7	27.0		± 10.3	± 11.4	± 16.9
36			3.8	6.8			± 5.2	± 9.3

Table IX. Investigation of the correlation between the studied parameters

Correlation	No of observation	Gamma	Z	p
Stage & treatment	744	0.255089	6.78522	0.000000
Stage & chemotherapy	200	0.083491	1.21594	0.224006
Status & treatment	744	0.093067	2.44633	0.014432
Status & chemotherapy	200	0.073177	0.94004	0.347195
Sex & treatment	744	0.106212	2.67540	0.007464
Sex & chemotherapy	200	0.043430	0.55040	0.582047
Localization & treatment	744	0.675667	15.94777	0.000000
Localization & chemotherapy	200	0.192712	2.29974	0.021463

ANALYSIS OF THE CUMULATIVE SURVIVAL RATE OF PATIENTS WITH STAGE IV RECTAL CANCER (RC)

There were 13.5% of patients (105 people) with stage IV rectal cancer. 88 patients have undergone special treatment (83.8%). Surgery was received by 31 patients (29.5%), surgery + chemotherapy – by 19 people (18.1%), chemotherapy – by 13 people (12.4%) and radiation therapy – by 11 patients (10.5%). 8 patients received surgery + chemotherapy + radiotherapy (7.6%) and 3 patients (2.9%) received surgical + radiation and chemotherapy + radiotherapy (Fig. 7).

Analysis of the indicator of cumulative survival of patients depending on the treatment received (Fig. 8).

According to the calculations $p = 0.0000$, which indicates the effect of treatment method on the cumulative survival rate of patients.

Overall survival (%) of patients with stage IV rectal cancer depending on method of treatment (Table VIII).

Higher survival rates were seen in patients with stage IV rectal cancer, who received surgery + chemotherapy and chemotherapy.

The lowest survival rates of patients with surgery were seen in each of the intervals studied. On the 12th month of observation, this indicator was only 5.4%, compared with 50.4% in patients, who received chemotherapy and 68.1% in patients with surgery+ chemotherapy.

6.8% patients received chemotherapy, 3.8% – surgery + chemotherapy. There were no patients with surgery or radiotherapy only at this stage of observation.

According to the results we can say that chemotherapy in the treatment of rectal cancer is effective for patients with stage IV rectal cancer.

DISCUSSION

Despite the latest diagnostic methods, immunohistochemical studies, microsatellite instability and modern

treatments based on the molecular profile of the tumour, the results of survival of patients with colorectal cancer remain unsatisfactory, which encourages scientists to continue studying this pathology. Patients with stage II colorectal cancer (RC) are of particular interest, as the choice of adjuvant treatment for these patients depends on negative prognostic factors.

To summarize the results of the study, a correlational relationship between the studied parameters was identified (Table IX).

The marked correlations are significant, at $p < 0.05000$.

There is a correlation between:

- stage and treatment;
- status (died / registered) and treatment;
- status and treatment;
- localization and treatment.
- localization and chemotherapy.

According to the literature, females with stage I-III disease are more prognostically favorable in comparison with males and have better prognosis for survival [15].

According to the study by Dossa F., Acuna S.A., patients who received adjuvant chemotherapy showed better overall survival for 5 years than those who did not receive adjuvant treatment (95.0% vs. 88.2%) [16].

Rectal cancer is currently one of the most common malignant tumors both in Ukraine and in the world.

Despite the latest diagnostic methods, immunohistochemical studies, microsatellite instability and modern treatments, the overall survival of patients remains unsatisfactory.

Even within homogeneous groups of patients, rectal cancer is characterized by a high heterogeneity of the course and response to therapy, which necessitates a more detailed retrospective analysis of case histories and the study of prognostic factors.

CONCLUSIONS

According to the obtained results, the overall survival of patients correlates with the stage of rectal cancer: we see the highest survival rates in patients with stage II RC and, accordingly, and the lowest – in stage IV RC in each of the studied time intervals.

The use of combined and integrated treatment in patients with stages II and III RC gives a higher rate of cumulative survival of patients at each of the studied intervals.

In step-by-step analysis:

- stage II RC: on the 5th year of observation, the overall survival rate of patients was 8.4%, 1.6% and 7.7% respectively in patients, who received surgery, radiotherapy or chemotherapy; similar indicators were seen in patients with surgery + radiation therapy, surgery + radiation therapy + chemotherapy and surgery + chemotherapy – 45.6%, 21.1%, and 30%;

- stage III RC: on the 3rd year of observation the overall survival rate of patients with surgery was 14.1% against 45.4% and 32.4% in patients with a combined treatment (surgery + radiation therapy) and complex treatment (surgery + radiotherapy + chemotherapy) respectively.

For patients with stage IV RC the use of chemotherapy shows a significantly higher rate of cumulative survival of patients. On the 3rd year of observation, 6.8% of patients received chemotherapy – and 3.8% – surgery + chemotherapy.

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Conflict of interest:

The Authors declare no conflict of interest.

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A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis,
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