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Remote Results of Treatment of Patients with Colorectal Cancer against the Background of Inflammatory Bowel Diseases

Asatullayev A.
PhD of oncology department

Muminov B., Khakimov R.
Resident intern of the oncology department

Annotation: To compare overall and relapse-free survival of patients with sporadic colorectal cancer (CRC) and patients with CRC associated with inflammatory bowel disease (IBD).

in a group of patients with CRC and IBD (n=17) and a group of patients with sporadic CRC (n=17), the overall and relapse-free survival rates, perioperative parameters (complications, number of removed and affected lymph nodes, duration of hospitalization in the postoperative period) were assessed.

patients in both groups did not differ statistically significantly in the duration of surgery, volume of intraoperative blood loss, frequency of postoperative complications and duration of hospitalization. No significant differences in the progression of oncological disease were found. Overall survival for 1 year was 100% in the group of patients with CRC and IBD and 94.2% in the group with sporadic CRC, relapse-free survival was 71 and 79%, respectively, and cancer-specific survival was 100% in both groups. The predicted 3-year indicators were 68 and 94.2% for overall survival, 75 and 79% for relapse-free survival, 68 and 100% for cancer-specific survival in the CRC and IBD groups and with sporadic CRC, respectively. According to the obtained data, IBD is not an unfavorable factor for overall and cancer-specific survival in patients with CRC: clinical characteristics, perioperative data and oncologic outcomes in patients with CRC and IBD did not differ from those in patients with sporadic CRC. Previous studies on the oncologic outcome of IBD-associated CRC and sporadic CRC have shown conflicting results, which may be due to the use of non-representative databases. Our study is also limited by a small number of patients, follow-up time and retrospective single-center design, which allows only preliminary conclusions.

Clinical outcomes in patients with CRC and IBD are similar to those in patients with sporadic CRC. The impact of IBD on long-term oncological outcomes remains an open question. Multicenter studies and accumulation of clinical data are needed.

Keywords: colorectal cancer, inflammatory bowel disease, Crohn's disease, ulcerative colitis, relapse, oncology.

Introduction: According to GLOBOCAN (Global Cancer Observatory), colorectal cancer (CRC) ranks third in incidence and second in mortality among oncological diseases worldwide [1]. Well-known risk factors for CRC include age, male gender, smoking, excessive alcohol consumption, physical inactivity, high consumption of red and processed meat, excess body weight, family history of CRC and inflammatory bowel disease (IBD). Chronic inflammation of the intestinal wall is known to be one of the main non-modifiable factors increasing the risk of CRC [2]. According to a meta-analysis, the risk of CRC in patients with IBD is 2% after 10 years, 8% after 20 years, and 18% after 30 years from the onset of the disease [3]. Moreover, the duration, degree and severity of IBD, the presence of inflammatory pseudopolyps and primary sclerosing cholangitis increase the risk of developing CRC and worsen the prognosis of the disease [4].

Data from one population-based study showed that patients with IBD who undergo regular screening have lower mortality rates and higher 3-year disease-free survival compared with patients who do not participate in screening programs.

Objective: To compare overall and relapse-free survival in patients with sporadic CRC and in patients with IBD-associated CRC.

Material and methods

A retrospective case-control study was conducted in the Proctology Department of the A.S. Loginov Moscow Cancer Research Center. Two groups of patients were formed. The main group (CRC + IBD) included 19 patients with CRC that developed against the background of IBD, with a known outcome of the disease in the period 2014-2022. Subsequently, 2 patients of the main group were excluded from the study due to the lack of data on their current condition. Based on information on age, gender, stage of the tumor process and clinical and anamnestic data from the prospectively filled database of the A.S. Loginov Moscow Cancer Research Center, Department of Health of the City of Moscow, 17 patients with sporadic CRC were individually selected for the comparison group (sCRC).

The primary endpoint of the study was overall and relapse-free survival; the secondary endpoint was perioperative parameters (frequency and type of postoperative complications, number of removed and affected lymph nodes, and duration of hospitalization in the postoperative period). Statistical analysis was performed using IBM SPSS Statistics for mac software (SPSS: An IBM Company, USA). Pearson and Mann-Whitney tests were used for categorical variables and Student's t-test for quantitative variables.

Research results

Table 1 presents the clinical and anamnestic characteristics of patients in both groups.

Table 1. Clinical and anamnestic characteristics of patients of both groups in the preoperative period

Parameter		KPP + B3K (n=17)	cKPP (n=17)	p
Age, years		50.7±15.2	55.1±13.3	>0.05
Floor: male, n (%) female, n (%)		8 (47) 9 (53)	8 (47) 9 (53)	1,000
Age at diagnosis of CRC, years		49.4±14.7	53.4±12.9	0.418
BMI, p (%): <30 kg/m² ≥30 kg/m²		17 (100) 0	16 (94.12) 1 (5.88)	0.317
Hemoglobin, n (%): >80 g/l <80 g/l		17 (100) 0	17 (100) 0	1,000
CRP, p (%): ≤5 mg/l >5 mg/l		14 (82.35) 3 (17.65)	13 (76.47) 4 (23.53)	0.279
Tumor localization, n (%): colon rectum anal canal		12 (70.59) 4 (23.53) 1 (5.88)	12 (70.59) 5 (29.41) 0	0.914
Tumor symptomatology, n (%)		4 (23.5)	13 (76.4)	0.005
REA, p (%): ≤5 ng/ml >5 ng/ml		14 (82.35) 3 (17.65)	12 (70.59) 5 (29.41)	0.426
Neoadjuvant chemo-/chemo-radiotherapy, n (%)		1 (5.88)	3 (17.65)	0.601
TIM assessment, p (%)				
pT	2	3 (17.6)	3 (17.6)	1,000
	3	10 (58.82)	10 (58.82)	
	4	3 (17.6)	3 (17.6)	
pN	0	5 (29.41)	5 (29.41)	0.838
	1	9 (52.94)	9 (52.94)	
	2	2 (11.76)	2 (11.76)	
C.M.		3 (17.6)	3 (17.6)	1,000

Note: BMI – body mass index, CRP – C-reactive protein, CEA – carcinoembryonic antigen.

Patients in both groups did not differ in gender, age, BMI, tumor stage, hemoglobin level, and CRP ($p>0.05$). There were no differences in the number of patients receiving neoadjuvant treatment. It is worth noting that in the overall sample of patients, colon cancer was diagnosed more often than rectal or anal cancer (71% versus 29%, respectively).

Of 17 patients in the CRC + IBD group, 13 (76%) were diagnosed with ulcerative colitis (UC), and 4 (24%) with Crohn's disease, which explains the higher risk of malignancy in case of total intestinal involvement. However, despite the early manifestation of IBD, the differences in the average age of patients at the time of diagnosis of CRC that developed against the background of IBD (49.4 ± 14.7 years) and sporadic CRC (53.4 ± 12.9 years) were statistically insignificant ($p = 0.418$). Tumor symptomatology at the time of CRC diagnosis was noted in 4 (23.5%) patients in the CRC + IBD group and in 13 (76.4%) patients in the sCRC group ($p = 0.005$). This fact is probably due to the fact that patients with IBD constitute a group of opportunistic screening with colonoscopy, as well as the prevalence of IBD symptoms over CRC symptoms.

During the preoperative follow-up examination, the CEA content was of greatest interest, but no significant differences in this indicator were found between the groups. The groups also did not differ in the number of patients with increased BMI, anemia, and neoadjuvant chemotherapy.

The groups did not differ in the main intraoperative and postoperative parameters, such as the duration of surgery, the volume of blood loss and the incidence of complications (Table 2). The volume of operations differed significantly: patients with CRC + IBD more often underwent more extensive interventions (colectomy/colproctectomy), while in the sCRC group, segmental resections were more often performed ($p = 0.003$).

Table 2. Intraoperative and postoperative characteristics of patients in both groups

Parameter	KPP + B3K (n=17)	cKPP (n=17)	p
Operational access, n (%): laparotomy laparoscopy	5 (29.41) 12 (70.59)	3 (17.6) 14 (82.35)	0.419
Operation duration, min	220.5±70	176.7±75.7	0.090
Intraoperative blood loss, n (%): <200 ml >200 ml	16 (94.12) 1 (5.88)	16 (94.12) 1 (5.88)	1,000
Radicality of the operation, n (%): R01	17 (100)	17 (100)	1,000
Average number of lymph nodes found in the preparation, M±m	43.8±72.9	19.5±7.5	0.195
Average number of affected lymph nodes, M±t	1.8±2.4	1.1±1.1	0.323
Number of bed days, M±t	10.5±5.7	8.8±2.5	0.254
Class of complications in the postoperative period (Clavien-Dindo), n (%): without complications ≥IIIb	12 (70.59) 1 (5.88)	17 (100) 0	0.253

Pathomorphological examination of the preparations showed that in both groups, radical surgery was performed in 100% of cases (p=1.000); there was no significant difference in the average number of lymph nodes removed and examined (p=0.195), or affected (p=0.323).

Table 3 presents the immediate and long-term results of treatment.

Table 3. Treatment results for patients in both groups

Parameter	KPP + B3K (n=17)	cKPP (n=17)	p
Volume of surgical treatment, n (%): radical palliative	16 (94.12) 1 (5.88)	16 (94.12) 1 (5.88)	1,000
Type of surgical treatment, n (%): segmental resection colectomy/colproctectomy	10 (58.82) 7 (41.18)	0 17 (100)	0.003
Further treatment, n (%): observation adjuvant chemotherapy	7 (41.18) 10 (58.82)	5 (29.41) 12 (70.59)	0.473
Relapse, n (%)	4 (23.53)	3 (17.65)	0.671
Disease progression n (%): local relapse metastases combination	2 (11.76) 2 (11.76) 0	0 2 (11.76) 1 (5.88)	0.155
Fatal outcome, n (%)	1 (5.88)	1 (5.88)	1,000
Cause of death, n (%) underlying disease other reasons	1 (5.88) 0	0 1 (5.88)	0.157
Median follow-up, months	14	18	0.493

According to the results of the pathomorphological examination and final staging of the oncological process, 10 (58.82%) patients in the CRC+IBD group and 12 (70.59%) patients in the sCRC group received adjuvant chemotherapy in the postoperative period (p=0.473).

The groups did not differ in the number of patients with cancer progression (23.53 and 17.65%, p=0.671). Local relapse developed in 2 (11.76%) patients in the CRC + IBD group, there were no relapses in the sCRC group. The groups did not differ in the frequency of distant metastasis (11.76 and 11.76%). The combination of local relapse and the appearance of distant metastases was recorded in 1 (5.88%) patient in the sCRC group. There was no significant difference in the rates of cancer progression in the groups (p=0.155).

In the CRC + IBD group, the minimum follow-up period was 1 month, the maximum was 72 months, and the median follow-up was 14 months. In the control group, the follow-up period ranged from 3 to 61 months, with a median of 18 months (p = 0.493). Considering that the median follow-up in both cases did not reach 2 years, the true one-year overall, cancer-specific, and relapse-free survival were calculated. The true one-year overall survival (Fig. 1) in the CRC + IBD group was 100%, while in the sCRC group it was 94.2%, and the relapse-free survival (Fig. 2) was 71 and 79%, respectively (the survival in both groups did not differ, p = 0.700). Cancer-specific one-year survival (Fig. 3) in both groups was 100%.

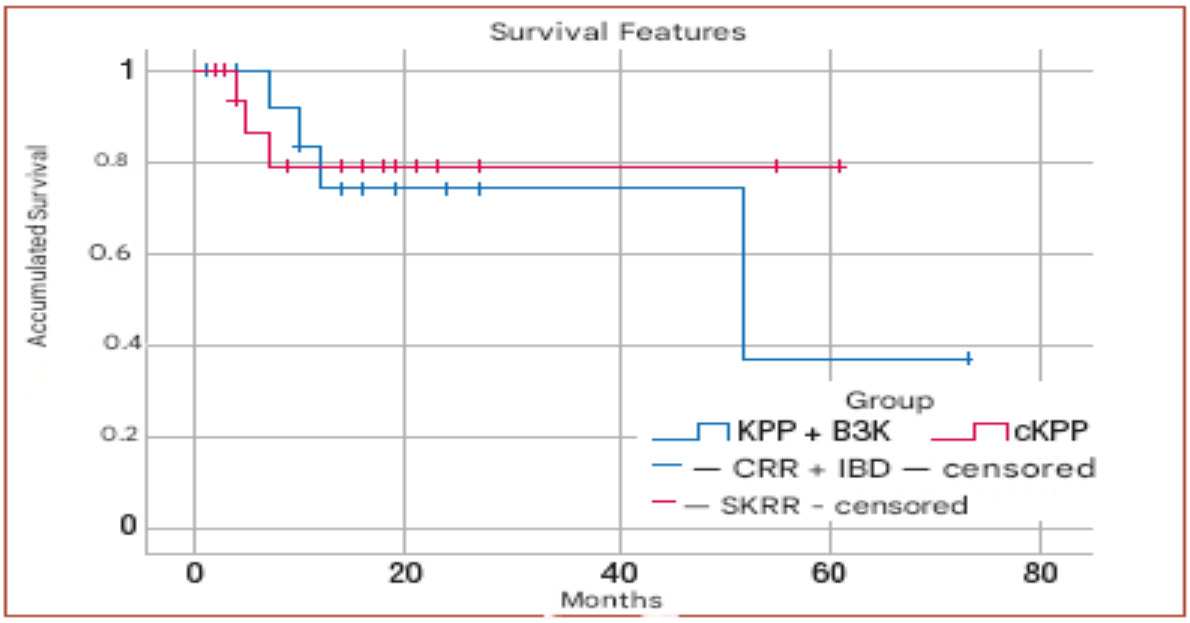

Fig. 2. Kaplan-Meier curves showing relapse-free survival of patients in both groups, with comparison using the log-rank test

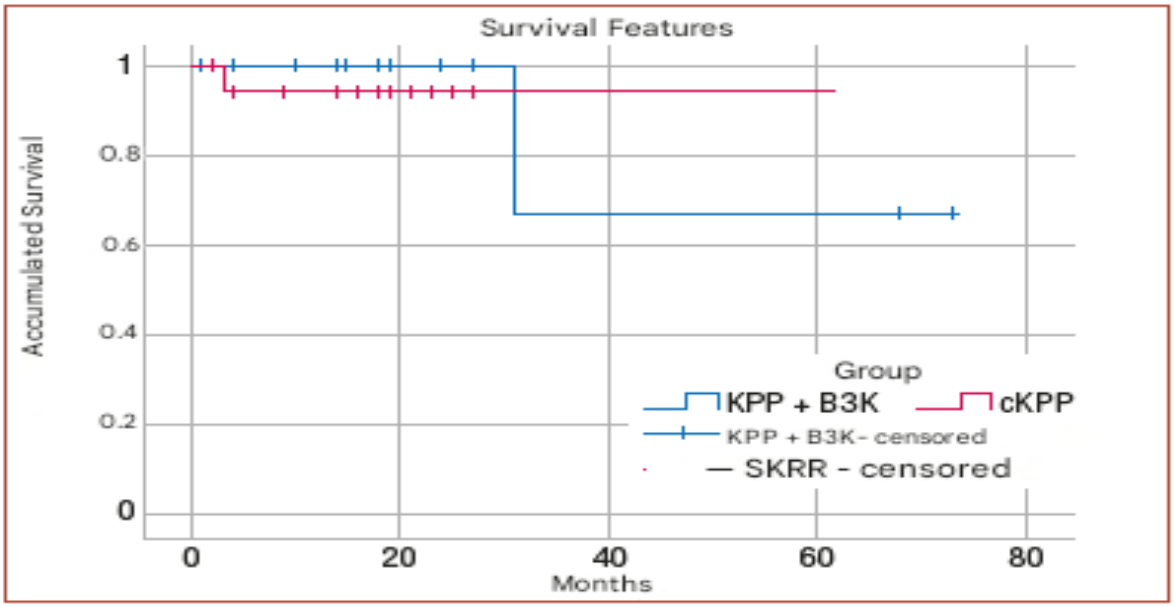

Fig. 1. Kaplan-Meier curves showing overall survival of patients, with comparison by log-rank test

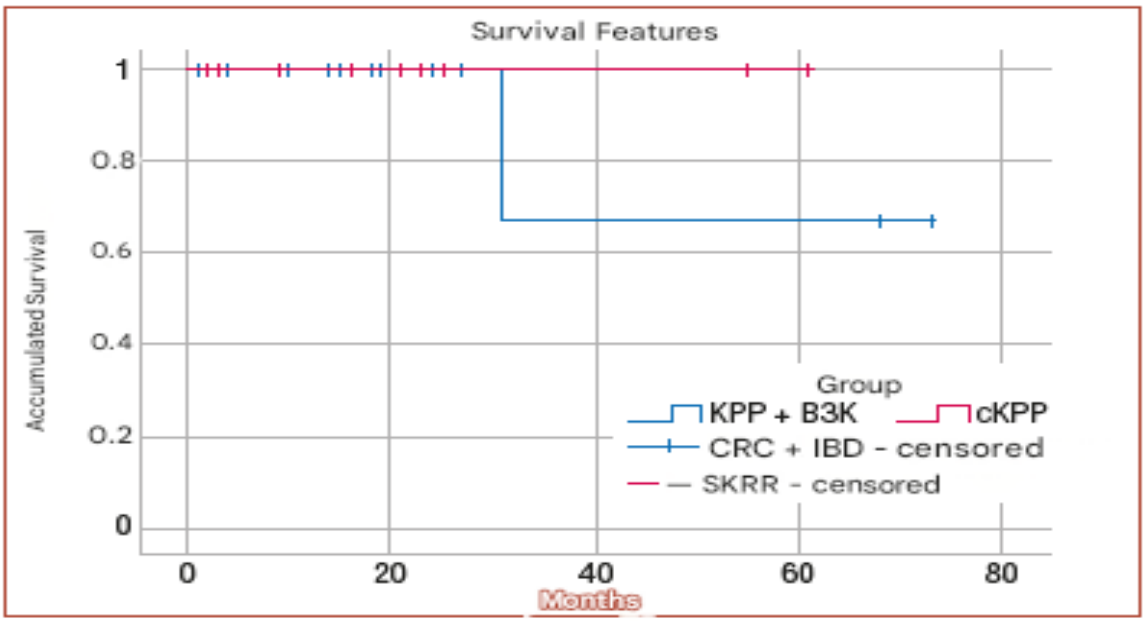

Fig. 3. Kaplan-Meier curves showing cancer-specific survival of patients in both groups, with comparison using the log-rank test

The predicted 3-year rates for the CRC + IBD and sCRC groups were 68 and 94.2% for overall survival, 75 and 79% for relapse-free survival, and 68 and 100% for cancer-specific survival, respectively (see Figs. 1–3).

According to the Kaplan-Meier curves and the log-rank test, IBD is not an unfavorable prognostic factor for either overall (p=0.945) or cancer-specific (p=0.414) survival in patients with CRC.

Discussion

Given that the risk of developing CRC in patients with IBD is increased [1–3, 11], the oncology community faces the question of the need for more careful monitoring of patients after surgery.

The presented study analyzed the overall, relapse-free, and cancer-specific survival rates. The results of the study suggest that the presence of IBD in a patient with CRC does not have a significant impact on the long-term treatment results. In addition, no differences were found in relation to many other factors. The extent of surgical treatment, the duration of surgery, the use of pre- or postoperative chemotherapy / chemoradiation therapy, the frequency of severe complications, the length of hospital stay, and other factors did not significantly affect the treatment outcome.

Previous studies comparing oncologic outcomes of IBD-associated CRC and sporadic CRC have shown conflicting results.

Thus, according to the results of one of the latest studies by Y.Z. Qwaider et al. [6], conducted in the USA in 2021, there were no differences in the outcomes of CRC treatment in patients with IBD compared to patients with sporadic cases of CRC. According to the study by T. Delaunoit et al. [7], at the Mayo Clinic, survival rates for IBD-associated CRC and sporadic CRC were similar. After analyzing the results of a population-based study in Central Asia. [8] concluded that, despite the fact that the characteristics of patients with CRC and IBD differ significantly from the characteristics of patients with CRC without IBD, each group of patients receives similar treatment and has similar patterns of disease progression after diagnosis.

At the same time, the conclusions based on the results of a number of other studies differ radically. Thus, T. Watanabe et al. [9] analyzed the prognosis and clinicopathological features of CRC associated with UC (UC-CRC) compared with sporadic CRC in the Japanese population. Based on the review data, it was shown that survival among patients with UC-CRC is lower than among patients with

sporadic CRC at a late stage of the disease, but no differences were observed at an early stage. The researchers concluded that early diagnosis of UC-CRC will allow one to expect postoperative results similar to the results of surgical treatment of sporadic CRC. These data emphasize the importance of early detection of UC-CRC. A.B. Jensen et al. [10] came to similar conclusions when analyzing the prognosis of the course of UC-CRC compared with CRC without UC.

It is worth considering that these discrepancies may be due to the use of suboptimal and non-representative databases.

Our study is also limited by the small number of patients, the duration of follow-up, and the retrospective design of a single center study, which means that only tentative conclusions can be drawn from the results.

In the present study, clinical characteristics, perioperative data, and oncologic outcomes did not differ between patients with CRC and concomitant IBD and patients with sporadic CRC.

Conclusion

The impact of IBD on long-term outcomes of CRC treatment remains an issue that requires further study. Our study showed that the presence of IBD in patients with CRC is not a significant prognostic factor for overall and relapse-free survival and does not significantly affect oncological outcomes. However, the limited sample size and retrospective study design require caution in interpreting the data. Multicenter studies with a larger number of patients and a long-term follow-up period are needed to more accurately understand and confirm these results. Additional studies will optimize the management strategy for patients with CRC against the background of IBD.

Literature

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