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Original Article

Laparoscopic radical resection combined with neoadjuvant chemotherapy in treatment of colorectal cancer: clinical efficacy and postoperative complications

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Abstract: Objective: To explore the clinical efficacy of laparoscopic radical resection combined with neoadjuvant chemotherapy (NACT) in the treatment of colorectal cancer and its influence on postoperative complications. Methods: The clinical data of 90 patients with colorectal cancer admitted to our hospital from June 2019 to June 2021 were retrospectively analyzed. According to different treatment methods, patients were divided into a control group (laparoscopic radical resection) and a study group (combined NACT before radical resection), with 45 cases in each group. The efficacy and complications were compared between the two groups after treatment. Results: Postoperatively, the early oral feeding, anal exhaust time, and hospitalization time of the patients in the study group were significantly shorter than those in the control group ($P<0.05$). The study group had significantly lower cancer metastasis rate, recurrence rate, infection rate, and smaller tumor diameters than the control group ($P<0.05$). The levels of tumor markers (CEA, CA242, CA199, and CA724) were reduced significantly in both groups after treatment, with lower results observed in the study group ($P<0.05$). The average survival time of patients in the study group was significantly longer than that of the control group (16.04±3.64 vs 11.88±2.53 months; $t=6.295$, $P<0.001$). The two groups showed no significant differences in the incidence of complications ($P>0.05$). Conclusion: Laparoscopic radical resection of colorectal cancer combined with NACT is a preferred technique for the treatment of colorectal cancer. It effectively facilitates the postoperative recovery, reduces the levels of tumor markers, boosts the short-term curative effect, and prolongs the average survival time, without obvious complications.

Keywords: Laparoscopy, colorectal cancer, neoadjuvant chemotherapy, complications

Introduction

It has been reported that colorectal cancer is the third most common malignant tumor and the second-leading cause of cancer-related death [1-3]. The incidence of colorectal cancer has witnessed an increasing trend in recent years, which has captured extensive clinical attention. At present, surgery is the mainstay for treating colorectal cancer, in which minimally invasive laparoscopic surgery is preferred by patients. However, given the common late diagnosis of patients, the postoperative survival time of patients is unsatisfactory after laparoscopic radical surgery [4-6]. Since the 1980s, neoadjuvant chemotherapy (NACT), adjuvant therapy for perioperative colorectal cancer, has achieved remarkable results in inhibiting disease progression [7-9]. Adjuvant chemotherapy induces apoptosis of cancer cells, reduces primary foci, decreases tissue reactive edema, and attenuates tumor adhesions to surrounding tissues [9]. The clinical effect of laparoscopic surgery combined with neoadjuvant radiotherapy for colorectal cancer has been reported to exceed that of stand-alone laparoscopic surgery [10-12]. Neoadjuvant chemotherapy drugs mainly include three cytotoxic drugs and two targeted drugs. For colorectal cancer, targeted drugs include epithelial growth factor receptor inhibitors, cetuximab, and bevacizumab. The combination of chemotherapeutic drugs and targeted drugs can shrink unresectable tumors to a resectable size. The merit of NACT lies in

the following: (1) NACT downsizes tumors and metastatic foci, especially lung metastasis, to facilitate surgical resection and limb preservation. (2) NACT postoperatively reduces the size or activity of tumor cells, lowers the incidence of metastasis and postoperative complications, and facilitates postoperative recovery. (3) NACT prevents the occurrence of distant metastases at an early stage and improves long-term survival rate. (4) NACT is the best in vivo site for drug sensitivity testing, which may provide a basis for future adjuvant therapy. Accordingly, this study evaluates the effect of laparoscopic radical resection of colorectal cancer combined with NACT on disease progression and postoperative recovery of patients by observing the levels of tumor markers, and the short- and long-term efficacy.

Materials and methods

Patient selection and grouping

The clinical data of 90 patients with colorectal cancer admitted to our hospital from June 2019 to June 2021 were retrospectively analyzed. According to different treatment methods, patients were divided into a control group (laparoscopic radical resection) and a study group (combined NACT before radical treatment), with 45 patients in each group. The ethics committee of our hospital has approved the study. The ethics approval number is 2019-05-26.

Inclusion criteria

(1) Patients with a colorectal cancer diagnosis by histopathologic examination, colorectal endoscopy, and tumor markers; Pathological biopsy to clarify the characteristic of occupancy is the diagnostic criterion of colorectal cancer; (2) Patients with a life expectancy of >3 months; (3) Patients with complete medical records and a high compliance; (4) Patients and their families were informed of the purpose and process of this study, and signed a consent form; (5) Patients had thick and bloody stools after infection; (6) Patients had chronic intestinal obstruction, abdominal distension, hyperacusis, and paroxysmal colic; (7) Patients had loss of appetite, emaciation, fatigue, anaemia, jaundice, or ascites; (8) Patients had altered bowel habits, purulent stools, urgency, constipation, and diarrhea.

Exclusion criteria

(1) Patients with severe organic diseases (liver, kidney, heart, and lung) or malignant tumors; (2) Patients with hematologic diseases or infectious diseases; (3) Patients with a tumor diameter of ≥6 cm; (4) Patients with intolerance to chemotherapy drugs.

Methods

After admission, all patients received routine treatments for colorectal cancer based on their conditions, including routine interventions for underlying diseases and nutritional support [10-13]. Control group: Patients with determined surgical tolerance were scheduled for laparoscopic surgery. After general anesthesia, artificial pneumoperitoneum was established with appropriate pneumoperitoneum pressure, and the umbilicus was perforated to clarify the location of the tumor. Radical resection was performed to remove all the tumors visible to the naked eye, including the primary foci and the lymph nodes in the drainage area. According to the location of the tumor, the left hemicolectomy, right hemicolectomy, or transverse colon were selectively resected. Anti-infection and nutritional support treatment were provided postoperatively. The scope of tumor tissue resection was determined by referring to the *Laparoscopic Colorectal Cancer Surgery Standard Guidelines*. The tissue specimens were removed for pathological examination. Research group: Preoperatively, all patients received four 14-day courses of NACT with FOLFOX4. Blood and urine routine, electrocardiogram, tumor markers, lactate dehydrogenase, and alkaline phosphatase were examined before every treatment cycle. After chemotherapy, symptomatic and supportive treatments such as stomach protection, liver protection, and anti-vomiting were given accordingly.

FOLFOX4 chemotherapy regimen: Patients were given an intravenous infusion of 400 mg/m^2 (dL) calcium leucovorin (specification: 100 mg according to C20H23N7O7, manufacturer: Yuekang Pharmaceutical Group Co., Ltd., SFDA Approval Number H20044158) and 400 mg/m^2 (dL) 5-Uracil (specification: 0.25 g, manufacturer: Shanghai Xudong Haipu Pharmaceutical Co., Ltd., SFDA Approval Number H31020593) both with an infusion time of >30 min. 100 mg/m^2 (dL) oxaliplatin (specification: 0.1 g, Manu-

Table 1. Comparison of general information in the two groups (n=45)

	Control group	Study group	χ^2/t	P
Age (year)	53.42±7.31	53.33±7.45	0.058	0.954
Gender			0.403	0.525
Male	23 (51.11)	26 (57.78)		
Female	22 (48.89)	19 (42.22)		
Tumor site			0.194	0.660
colon	17 (37.78)	15 (33.33)		
rectum	28 (62.22)	30 (66.67)		
Clinical stage (TNM)				
II	13 (28.89)	12 (26.67)	0.055	0.814
III	25 (55.56)	28 (62.22)	0.413	0.520
IV	7 (15.56)	5 (11.11)	0.385	0.535
Pathological grade				
Well differentiated	11 (24.44)	13 (28.89)	0.227	0.634
Moderately differentiated	26 (57.78)	27 (60)	0.046	0.830
Poorly differentiated	8 (17.78)	5 (11.11)	0.809	0.368
ASA grade				
II	10 (22.22)	11 (24.44)	0.062	0.803
III	29 (64.44)	30 (66.67)	0.049	0.824
IV	6 (13.33)	4 (8.89)	0.450	0.502

facturer: Qilu Pharmaceutical Co., Ltd., SFDA Approval Number H20093168) was also given intravenously, with an infusion time of >2 h, followed by continuous intravenous pumping of 2400-3000 mg/m^2 5-urafluridine, for 48 h. All patients received four courses of FOLFOX4 chemotherapy after surgery.

Outcome measures

Patients' general information such as age, gender, tumor sites, clinical staging (TNM staging standard [8]), pathologic type, and the American Society of Anesthesiologists (ASA) classification were recorded and compared. The early oral feeding, anal exhaust time, and hospital stay of patients after operation were recorded. The patients were re-examined after treatment to record and compare cancer cell metastasis, tumor diameter, recurrence, and infection in the two groups. The tumor diameter was measured in both longitudinal and transverse directions, and the larger diameter was determined as the tumor diameter. Before and after treatment, 8 mL of fasting morning intravenous non-anticoagulant blood was collected from patients and centrifuged at 3000 r/min for 10 min to obtain the serum. The serum carcinoembryonic antigen (CEA) level was determined using microparticle enzyme-linked immunoassay, the serum levels of carcinoembryonic antigen 242 (CA242) and carcinoembryonic antigen 199 (CA199) were determined using enzyme-linked immunosorbent assay, and the serum level of carcinoembryonic antigen 724 (CA724) was determined using electrochemiluminescence immunoassay. The occurrence of complications during treatment was counted in telephone follow-up and the efficacy in patients was analyzed.

Statistical analysis

The SPSS22.0 was used for data analysis, and GraphPad Prism 7 (GraphPad Software, San Diego, USA) was used for graphics plotting. Counted data and measured data, were represented by [n (%)] and ($\bar{x}$±s), respectively, and examined by χ^2 test. The paired t-test was used for intra-group comparisons, and the t-test for two independent samples was used for inter-group comparisons. Survival curves were plotted using the K-M method. *P* value <0.05 indicates that a difference is significant.

Results

General information

No significant difference was found in general data between the two groups (P>0.05), indicating the feasibility for a controlled experimental study, as shown in **Table 1**.

Postoperative recovery

The postoperative early oral feeding, anal exhaust time, and hospitalization time of patients in the study group were significantly shorter than those in the control group (P<0.05), as shown in **Table 2**.

Short-term efficacy

The study group had a remarkably lower cancer cell metastasis rate, recurrence rate, and infec-

Table 2. Surgical conditions of the two groups of patients ($\bar{x}\pm s$)

Group	Postoperative early oral feeding	Anal exhaust time (d)	Hospital stay (d)
Control group	6.92±1.43	3.61±1.17	22.34±2.45
Study group	5.58±1.67	2.58±1.12	16.59±2.07
t	4.089	4.266	12.026
P	<0.001	<0.001	<0.001

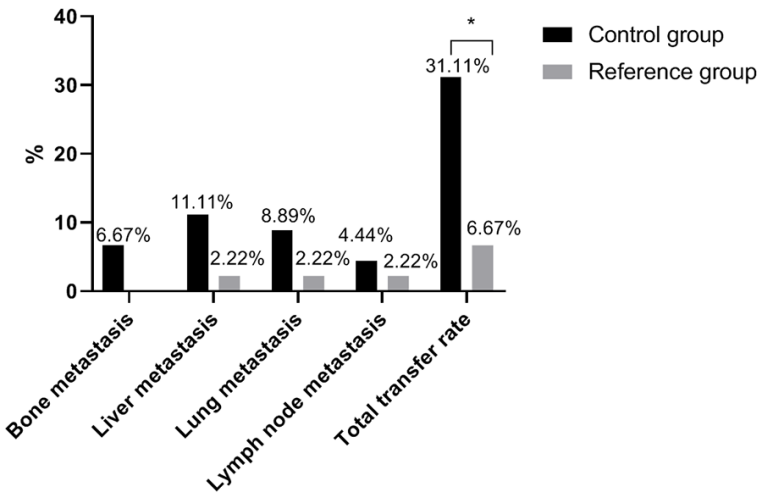

Figure 1. Comparison of cancer cell metastasis between the two groups (%). Note: The abscissa represents bone metastasis, liver metastasis, lung metastasis, lymph node metastasis and total metastasis rate, and the ordinate represents percentage, %; In the control group, there were 3 cases of bone metastasis, 5 cases of liver metastasis, 4 cases of lung metastasis, and 2 cases of lymph node metastasis, with a total of 14 cases; In the study group, there were 0 cases of bone metastasis, 1 case of liver metastasis, 1 case of lung metastasis, and 1 cases of lymph node metastasis, with a total of 3 cases; *indicates that the total metastasis rate of cancer cells between the two groups is significantly different (χ^2=8.775, P=0.003).

Table 3. Recurrence rate and infection rate in the two groups [n (%)]

Group	n	Tumor diameter (mm)	Recurrence rate	Infection rate
Control group	45	35.85±1.02	10 (22.22)	8 (17.78)
Study group	45	32.33±1.15	2 (4.44)	1 (2.22)
χ^2		15.361	6.154	6.049
P		<0.001	0.013	0.014

tion rate than the control group (P<0.05), as shown in **Figure 1** and **Table 3**.

Tumor marker levels

After treatment, the levels of tumor markers (CEA, CA242, CA199, CA724) decreased significantly in both groups, with lower results observed in the study group compared with the control group (P<0.05), as shown in **Table 4**.

Long-term efficacy

The average survival time of patients in the study group was markedly longer than that in the control group (16.04±3.64 vs 11.88±2.53 months; t=6.295, P<0.001), as shown in **Figure 2**.

Complications

The incidence of complications was not significantly different between the two groups (P>0.05), as shown in **Table 5**.

Discussion

Colorectal cancer is a common malignancy with no specific symptoms in the early stage, predisposing the disease to the middle and advanced stages at the time of diagnosis and the missing of optimal treatment timing, which results in a poor postoperative five-year survival rate [14-16]. Surgical treatment combined with adjuvant radiotherapy and chemotherapy is a favorable treatment method for patients at the advanced stages of the disease. In recent years, laparoscopic surgery has gradually replaced traditional open surgery in the field of bowel cancer, as the former with minimal invasion accurately determines the location and disease level of the tumor, improves the total resection rate, and minimizes the wound area [17-20].

However, surgery fails to achieve complete removal of cancer cells, with a high risk of postoperative recurrence, which necessitates appropriate radiotherapy and chemotherapy regimens. NACT refers to the systemic chemotherapy given to patients before surgery, which

Table 4. Levels of tumor markers in the two groups

		Control group	Study group	t/P
CEA (ng/ml)	Before treatment	10.15±3.37	10.26±3.45	
	After treatment	6.72±2.17	5.04±2.01	3.810<0.001
CA242 (IU/ml)	Before treatment	25.31±10.08	25.07±10.11	
	After treatment	19.12±6.73	14.88±6.52	3.035/0.003
CA199 (IU/ml)	Before treatment	43.08±15.44	43.30±14.97	
	After treatment	30.96±10.07	24.65±9.54	3.052/0.003
CA724 (IU/ml)	Before treatment	7.55±3.04	7.68±3.12	
	After treatment	5.38±1.25	4.17±1.08	4.914/<0.001

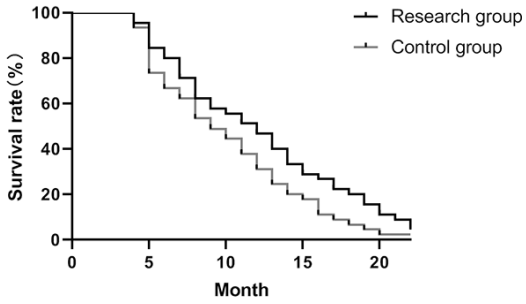

Figure 2. Survival time in the two groups.

shrinks the mass and kills the invisible metastatic cells. The combination of the two effectively reduces the local recurrence rate and improves the curative effect. Moreover, the detection of tumor markers serves to diagnose e tumors, monitor disease progression, evaluate treatment efficacy, and predict clinical outcome, especially in the treatment of colorectal cancer [21-24]. Remarkably, the present study showed significantly shorter postoperative early oral feeding, anal exhaust time, and hospital stay in the study group than those in the control group, which is consistent with the study results of BHANGU [25], indicating that laparoscopic radical resection of colorectal cancer combined with NACT can facilitate the postoperative recovery of patients. In terms of short-term efficacy, the cancer metastasis rate, recurrence rate, tumor diameter, and infection rate of the study group were significantly lower than those of the control group, suggesting that NACT combined with laparoscopic radical resection of colorectal cancer could significantly reduce the diameter of the tumor, which better contributes to the disease control and efficacy enhancement.

This study also found a greater reduction of CEA, CA199, and CA724 levels in the study group than those in the control group. CEA is a cell surface-related protein used to systematically evaluate the curative effect of patients after tumor metastasis. CA199, with no significant correlation with tumor type, location, or degree of cancer cell differentiation, present increased expression levels with the progression of colorectal cancer. CA724, a high molecular glycoprotein antigen with high sensitivity and specificity for colorectal cancer, directly reflects the degree of tumor invasion and lymph node metastasis, and also indicates the degree of tumor burden. Results from this study demonstrated that the combined application of NACT before laparoscopic radical resection of colorectal cancer can control the condition of the disease by affecting the expression of multiple tumor markers. The average survival time of patients in the study group was (16.04±3.64) months, significantly higher than that of the control group (11.88±2.53) months, which may be ascribed to the following reasons: (1) NACT preoperatively reduces the primary lesions and inhibits postoperative recurrence; (2) NACT effectively controls iatrogenic metastasis caused by laparoscopic surgery, thereby improving the long-term survival time of patients; (3) NACT assists high-dose drugs to kill tumors, thereby enhancing treatment efficacy. Moreover, the combination therapy features a high safety profile. The limitation of this study lies in minimal analysis of the prognostic status of patients including their quality of life and psychological status. Since chemotherapy use has a significant impact on postoperative patients' lives, appropriate psychological interventions contribute positively to patients' prognosis. Future studies will be conducted to investigate the patients' postoperative lives and psychology to obtain more clinical data.

Conclusion

Laparoscopic radical resection of colorectal cancer combined with NACT is a preferable approach for the treatment of colorectal cancer, which effectively facilitates the postoperative recovery and reduces the levels of tumor

Table 5. Postoperative complications in the two groups

	Control group	Study group	χ^2	P
Intestinal obstruction	2 (4.44)	1 (2.22)	0.345	0.557
Abnormal liver function	2 (4.44)	1 (2.22)	0.345	0.557
Anastomotic bleeding	2 (4.44)	2 (4.44)	0.000	1.000
Urinary retention	4 (8.89)	5 (11.11)	0.124	0.725
Sick and vomit	6 (13.33)	7 (15.56)	0.090	0.764
Hair loss	10 (22.22)	9 (20)	0.067	0.796

markers, while improving the short-term curative recovery and reduces the levels of tumor markers, while improving the short-term curative effect and prolonging the average survival time of patients without obvious adverse complications. However, anus cannot be preserved after low rectal cancer surgery and artificial stoma is required (no anastomosis is excluded).

Disclosure of conflict of interest

None.

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