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Original Research Article

Clinical effect of neoadjuvant chemotherapy combined with laparoscopic surgery for patients with colorectal cancer

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Abstract

Purpose: *To assess the clinical effect of neoadjuvant chemotherapy in combination with laparoscopic surgery in treating progressive colorectal cancer.*
Methods: *90 patients with colorectal cancer admitted to Hebei Yanda Hospital, Hebei Langfang, China between December 2020 and December 2021 were enrolled. The patients were randomly grouped into control and study groups. Control group underwent laparoscopic surgery while the study group underwent neoadjuvant chemotherapy in addition to laparoscopic surgery. Gastrointestinal function recovery time, tumor control effect, tumor marker level, and adverse reactions were investigated and compared between the two groups.*
Results: *Time to anal exhaust, time to first defecation, time to first solid food intake, and time to recover to normal bowel sounds were earlier in the study group compared to control group ($p < 0.05$). Study group exhibited a greater overall rate of tumor control response., while the rate of tumor lymphatic metastasis was also significant ($p < 0.05$). After treatment, the study group exhibited significantly lower levels of tumor markers compared to control group ($p < 0.05$). The occurrence of adverse reactions was not significant between the two groups ($p > 0.05$).*
Conclusion: *Neoadjuvant chemotherapy in conjunction with laparoscopic surgery in the treatment of progressive rectal cancer improves patient outcomes and enhances prognosis.*

Keywords: *Colorectal cancer, Laparoscopic surgery, Neoadjuvant chemotherapy, Adverse effect*

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INTRODUCTION

China has a high incidence of colorectal cancer, and the number of colorectal cancer and deaths related in China accounts for 18.6 % and 20.1 % of the total number of cases and deaths worldwide respectively [1]. Moreover, as people's living habits change, the incidence of colorectal cancer has continued to increase in recent years [2]. The current clinical treatment of colorectal cancer usually involves surgery, radiation, chemotherapy, and combined therapy, among which laparoscopic surgery has become increasingly popular due to its small invasion, high degree of safety, and targeted effect [3,4]. In progressive colorectal cancer, the primary tumor

lesion invades the plasma membrane or extra-plasma local lymph nodes by penetrating the muscular layer of the intestinal wall. Thus, for patients with this condition, simple laparoscopic surgery is prone to recurrence accompanied by metastasis, leading to a relatively low 5-year survival rate [5]. To enhance patients' clinical prognosis, combining neoadjuvant chemotherapy with laparoscopic surgery is an effective measure.

Neoadjuvant chemotherapy refers to the administration of chemical treatment after a tumor has been definitively diagnosed but before undergoing surgery or other anti-tumor therapies such as radiation. Initially used in advanced-stage breast cancer, neoadjuvant chemotherapy is typically administered before surgery in order to reduce the size of tumors and facilitate surgical conditions. The duration of chemotherapy in neoadjuvant chemotherapy is short.

This study investigated the clinical effect of neoadjuvant chemotherapy in combination with laparoscopic surgery in patients with progressive colorectal cancer.

METHODS

General information

A total of 90 colorectal cancer patients admitted to the Hebei Yanda Hospital, Hebei Langfang, China between December 2020 and December 2021 were selected. The patients were randomly and equally allocated into study and control groups. This research protocol received approval from the Ethics Committee of the Hebei Yanda Hospital, Hebei Langfang, China (approval no. 20220319014HB) and was conducted in line with the principles established in the declaration of Helsinki [6].

Inclusion criteria

Patients diagnosed with progressive colorectal cancer by imaging, laboratory and pathological examinations after admission, no previous history of radiotherapy or other adjuvant therapy treatment, having indications for neoadjuvant chemotherapy, and having signed the research consent form.

Exclusion criteria

Patients who develop liver or lung metastasis, have severe liver insufficiency and are allergic to chemotherapeutic drugs.

Treatments

Control group was treated with laparoscopic surgery [4]. Patients were positioned in a modified lithotomy position. The puncture point was established and the laparoscopic system was inserted. Thereafter, inferior mesenteric vessels were separated, the proximal part of the root was closed, surrounding fat and lymphatic tissues were removed, and the left colonic artery was preserved. The sigmoid colon and rectum were pulled up, total mesorectal excision of the rectum was performed with the pelvic fascias as the baseline, and the autonomic plexus was preserved. The rectum and colon were anastomosed intraperitoneally with the aid of an anastomat, and the intestinal canal and tumor were resected extraperitoneally.

Anti-infection and XELOX chemotherapy (combination of oxaliplatin and capecitabine) regimens were performed after surgery. Oxaliplatin was injected intravenously at 130 mg/m^2 on day 1. Patients also took capecitabine tablets orally at 1000 mg/m^2 from day 1 to day 14, twice daily. Treatment consisted of four cycles, with continuous medication for two weeks, followed by a one-week break between each cycle.

Study group was treated with neoadjuvant chemotherapy combined with laparoscopic surgery. Neoadjuvant chemotherapy was performed using mitomycin, 5-fluorouracil, and cis-platinum pre-operatively [7]. Patients received routine examinations before arterial perfusion chemotherapy. Angiography was performed on the patient's right femoral artery to clarify the blood supply to the tumor [8]. The tumor blood supply vessel was inserted with a micro-guide wire and injected with mitomycin at 4 mg/m^2, 5-fluorouracil at 600 mg/m^2, and cis-platinum at 40 mg/m^2. The tumor blood supply vessel was also cannulated and injected with 15 mL 40 % iodinated oil injection to prevent thrombus. Laparoscopic surgery was performed seven days after completion of arterial perfusion chemotherapy [9]. The surgical method and postoperative chemotherapy used were the same as those employed in control group.

Evaluation of parameters/indices

Gastrointestinal function

Gastrointestinal function included time to anal exhaust, time to first defecation, time to first solid food intake, and time to recover to normal bowel sounds were investigated.

Tumor control effect and tumor lymphatic metastasis rate

Tumor control effect and tumor lymphatic metastasis rate were compared. Evaluation criteria of tumor control effect [10] are as follows: Complete disappearance of tumor lesions was considered as complete remission (CR); 50 % reduction of tumor lesions was considered as partial remission (PR); no significant improvement of tumor lesions was considered as stable (S); increase of tumor lesions by 20 % or more, or appearance of new lesions was considered as progression (P). Total response rate (TR) was calculated using Eq 1.

TR = CR + PR …… (1)

Levels of tumor markers

Levels of tumor markers which include carbohydrate antigen 724 (CA724), carbohydrate antigen 242 (CA242), and carcinoembryonic antigen (CEA), were measured by electro-chemiluminescence before and after treatment were compared [11].

Adverse reactions

Occurrence of adverse reactions, such as nausea, vomiting, infections, intestinal obstruction, and decreased appetite, was also recorded.

Statistical analysis

Data was analyzed using Statistical Packages for Social Sciences (SPSS, version 21.0) software. Measurement data that followed a normal distribution were represented as mean ± standard deviation (SD) and tested using student t-test. Count data were presented in percentages and tested using chi-square test. $P < 0.05$ was considered statistically significant.

RESULTS

Patients' data

There were no statistically significant differences ($p > 0.05$) in patients' data such as gender, age, and cancer staging, between study and control groups (Table 1).

Recovery time of gastrointestinal function

Study group experienced significantly earlier anal exhaust, first defecation, first solid food intake, and recovery to normal bowel sounds after surgery compared to control group ($p < 0.05$) (Table 2).

Tumor control response and lymphatic metastasis rate

Tumor control response of study group was significantly higher compared to control group ($p < 0.05$). Additionally, study group had significantly lower rate of tumor lymphatic metastasis compared to control group ($p < 0.05$) (Table 3).

Tumor marker levels

Concentration of tumor markers did not differ significantly between study and control groups before treatment ($p > 0.05$). However, there was a significant decrease in the concentration of tumor markers in study group compared to control group after treatment ($p < 0.05$) (Table 4).

Table 1: Comparison of general data between two groups (N = 45)

Group	Gender (male/female)	Age (year)	Cancer staging (N)	
			Stage II	Stage III
Study group	23/22	51.33±2.88	23	22
Control group	24/21	51.27±2.83	26	19
t/X^2	0.942	0.157	0.865	
P-value	> 0.05	> 0.05	> 0.05	

Table 2: Comparison of clinical indicators (mean ± SD, N = 45)

Recovery time (days)	Study group	Control group	*T-value*	*P-value*
Time to anal exhaust	3.01±0.33	4.13±0.52	5.741	< 0.05
Time to first defecation	4.25±1.23	7.58±1.26	10.576	< 0.05
Time to recover to normal bowel sounds	3.56±1.69	5.68±1.61	7.653	< 0.05
Time to first solid food intake	5.73±1.08	9.35±1.06	13.177	< 0.05

Table 3: Comparison of tumor control response and lymphatic metastasis rate (N = 45 in each group)

Characteristics		Study group	Control group	X^2	*P-value*
Tumor control effect	Complete remission	15(33.33)	10(22.22)		
	Partial remission	20(44.44)	12(26.67)		
	Stable	7(15.56)	15(33.33)		
	Progression	3(6.67)	8(17.78)		
	Total response rate	35(77.77)	22(48.89)	10.576	< 0.05
Tumor lymphatic metastasis rate		3(6.67)	14(31.11)	7.653	< 0.05

Table 4: Tumor marker before and after treatment in study and control groups (mean ± SD, N = 45 in each group)

Group		Study group	Control group	*T-value*	*P*-value
CEA (ng/mL)	Before treatment	30.16±2.35	30.17±2.42	0.056	> 0.05
	After treatment	2.52±0.31	4.69±1.46	10.941	< 0.05
CA242 (U/mL)	Before treatment	28.73±3.26	28.72±3.27	0.180	> 0.05
	After treatment	10.40±1.56	17.33±2.23	6.299	< 0.05
CA724 (U/mL)	Before treatment	18.67±2.42	18.69±2.45	0.187	> 0.05
	After treatment	5.12±0.33	8.41±0.61	7.765	< 0.05

Table 5: Comparison of complications (N = 45)

Group	Study group	Control group	X^2	*P*-value
Nausea and vomiting	3(6.67)	1(0.22)		
Infection	0(0.00)	3(6.67)		
Intestinal obstruction	1(0.22)	3(6.67)		
Decreased appetite	1(0.22)	3(6.67)		
Total	5(11.11)	10(22.22)	0.441	> 0.05

Adverse reactions

Incidence of adverse reactions in study group was lower in study group compared to control group ($p > 0.05$) (Table 5).

DISCUSSION

Chemotherapy is required after radical laparoscopic colorectal cancer surgery to improve prognosis, but oxaliplatin and capecitabine (XELOX) chemotherapy regimen is not very safe due to significant toxic and side effects. Therefore, combination therapy becomes imperative to promote prognosis [12,13]. A study has shown that advanced colorectal cancer is poorly treated with laparoscopic surgery alone and postoperative chemotherapy. As a result, neoadjuvant chemotherapy can be performed preoperatively to shrink the lesion [14]. Neoadjuvant chemotherapy is a new adjuvant malignancy chemotherapy regimen, which is safer than traditional chemotherapy and effectively enhances the efficacy of laparoscopic surgery [15].

Arterial perfusion chemotherapy used in study group is a kind of neoadjuvant chemotherapy. The chemotherapeutic drug is placed in the tumor blood vessels via a micro-guide wire so that it rapidly enters the tumor tissue and exerts its effect. It reduces the combined weight of plasma proteins and medicines and strengthens chemotherapeutic efficacy [16].

The findings of this study indicated that gastrointestinal function recovered fast in study group after surgery, suggesting that neoadjuvant chemotherapy significantly accelerated postoperative recovery of gastrointestinal function in colorectal cancer patients to absorb nutrients and improve immunity. This finding is similar to outcomes observed in previous investigations [17]. Moreover, the study group exhibited a higher overall response rate in terms of tumor control compared to control group, while also demonstrating a lower incidence of tumor lymphatic metastasis. Incidence of adverse reactions in both groups was non-significant. All these results suggest that the combined regimen was more beneficial in controlling the patients' disease and did not increase adverse reactions. The reason for the above results may be that the chemotherapeutic drugs produced intracellular reductase activation to promote DNA depolymerization, antagonize DNA replication, and inhibit tumor progression so that the levels of tumor markers such as CEA, CA242, and CA724 were decreased [18].

As presented in this study, CEA, CA242, and CA724 levels in study group were significantly lower compared to control group ($p < 0.05$). The result suggests that combination of neoadjuvant

chemotherapy and laparoscopic surgery has the potential to reduce tumor marker levels, which is an aspect rarely reported in previous studies [19,20].

Limitations of this study

The shortcoming of this study is that it has a small sample size and a brief study period, potentially affecting the accuracy and credibility of study results. In subsequent investigation, the number of participants may be increased and the effect of neoadjuvant chemotherapy combined with laparoscopic surgery on the long-term prognosis of individuals diagnosed with intermediate progressive colorectal cancer investigated.

CONCLUSION

Combined utilization of neoadjuvant chemotherapy and laparoscopic surgery demonstrates efficacy in managing advanced colorectal cancer. It also helps patients to recover from post-operative delayed gastrointestinal tract function, and reduces tumor marker levels and tumor lymphatic metastasis rate without increasing adverse effects.

DECLARATIONS

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None provided.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Hongyan Ma and Yuhui Zhou contributed equally to this study and should be regarded as co-first authors.

Ethical Approval

This study was approved by the Ethics Committee of the Hebei Yanda Hospital, Hebei Langfang, China (approval no. 20220319014HB).

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

***Use of Artificial Intelligence/*Large Language Models**

None provided.

Use of Research Reporting Tools

None provided.

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