

A clinical study on the nutritional status of patients with locally advanced rectal cancer during chemo-radiotherapy



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BACKGROUND: Rectal cancer is one of the most common gastrointestinal malignancies, and most cases include locally advanced cancers at the time of diagnosis (stage II/III).

OBJECTIVES: The purpose of this study is to observe the dynamic changes in the nutritional status of patients with locally advanced rectal cancer during concurrent radiation therapy and chemotherapy and to evaluate the nutritional risk and incidence of malnutrition in these patients.

METHODS: A total of 60 patients with locally advanced rectal cancer were enrolled in this study. The 2002 Nutritional Risk Screening and Patient-Generated Subjective Global Assessment Scales (PG-SGA) were used to assess nutritional risk and status. The European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (QLQ) - C30 and QLQ-CR38 scales were used for the quality of life evaluation. Toxicity was evaluated using the CTC 3.0 standard.

RESULTS: The incidence of nutritional risk among these 60 patients was 38.33% (23 of 60) before and 53% (32 of 60) after concurrent chemo-radiotherapy. There were 28 patients in the well-nourished group, with a PG-SGA score of <2 points, and 17 patients in the nutrition-changed group, with a PG-SGA score of <2 points before and 2 points during and after chemo-radiotherapy. In the well-nourished group, the incidence of nausea, vomiting and diarrhea mentioned in the summary was lower and the expectations for the future (according to the QLQ-CR30 and QLQ-CR28 scales) were higher than in the undernourished group. The undernourished group required delayed treatment more often and experienced nausea, vomiting and diarrhea earlier and for longer than the well-nourished group. These results show that the quality of life of the well-nourished group was better.

CONCLUSIONS: There is a degree of nutritional risk and deficiency in patients with locally advanced rectal cancer. Chemo-radiotherapy increases the incidence of nutritional risk and deficiencies.

KEY WORDS: Enteral nutrition, Colorectal neoplasms, Quality of life, Chemo-radiotherapy, EORTC

Introduction

Rectal cancer is one of the most common gastrointestinal malignancies, and most cases include locally advanced cancers at the time of diagnosis (stage II/III). At present, the comprehensive mode of surgery treatment combined with chemo-radiotherapy has significantly improved the control rate of local tumors and the survival rate of patients, but chemo-radiotherapy can also cause toxic symptoms in patients, such as nausea, vomiting and diarrhea. These symptoms further increase the nutritional risk and the likelihood of nutritional deficiencies in patients^{1,2}. Therefore, more attention should

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be paid to issues related to the nutritional status and quality of life (QOL) of patients when undergoing chemo-radiotherapy.

Currently, Nutritional Risk Screening 2002 (NRS 2002) is commonly used for the nutritional evaluation of hospitalized patients in China, but Patient-Generated Subjective Global Assessment (PG-SGA) has also been widely promoted and used for cancer patients in recent years³. The PG-SGA was developed on the basis of a subjective general evaluation, including a patient self-evaluation and medical staff evaluation, on weight, eating status, symptoms, activity and physical function, the relationship between disease and nutritional needs, stress state and a physical fitness evaluation. It is currently the most useful and widely used evaluation tool to assess the nutritional status of cancer patients and has been widely used and promoted by the American Dietetic Association⁴. Changes in nutritional risk can be predicted and understood using a nutritional assessment⁵. The scales, including the Core-30 Quality of Life Questionnaire of the European Organization for Research and Treatment of Cancer (EORTC) (QLQ-C30), and the colorectal cancer-specific Quality of Life Questionnaire (QLQ-CR38), are also widely used in China and abroad to evaluate the nutritional status and quality of life of patients with colorectal cancer⁶.

There are many studies on the correlation between nutritional status and toxicity in patients with locally advanced rectal cancer, but most of these include retrospective studies⁷⁻⁹, but there are few prospective clinical studies focusing on nutritional status and quality of life of patients with locally advanced rectal cancer who received concurrent preoperative or postoperative chemo-radiotherapy.

Furthermore, the sample size was small, mainly for patients with preoperative concurrent chemo-radiotherapy, and there was no study on the nutritional status of patients with postoperative concurrent chemo-radiotherapy¹⁰. This study is a prospective observational study aimed at observing locally advanced rectal cancer, noting dynamic changes in nutritional status during concurrent chemo-radiotherapy, assessing nutritional risk and incidence of malnutrition in patients during treatment, analyzing nutritional status and therapeutic efficacy of patients before, during and after treatment, and toxic effects of chemo-radiotherapy. The relevance of QOL will provide a basis for a better nutritional intervention for patients with locally advanced rectal cancer in the future.

Materials and Methods

PATIENTS

Clinical data of patients with locally advanced rectal cancer who underwent concurrent preoperative or postoperative chemo-radiotherapy in the Abdominal Oncology

of the Affiliated Hospital of the Guizhou Medical University (Affiliated Cancer Hospital of Guizhou Medical University) from December 2017 to December 2018 were collected, and patients who met the inclusion criteria were included in the study for analysis. This study was carried out in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Affiliated Cancer Hospital of Guizhou Medical University. Informed consent was obtained from each participant.

INCLUSION AND EXCLUSION CRITERIA

Inclusion criteria: (1) pathologically diagnosed with rectal adenocarcinoma, (2) a clinical or pathological stage after radical surgery of T3-4 and/or N +, (3) a tumor within 12 cm of the anal axis, (4) patients of any gender aged 18-70 years, and (5) a Karnofsky performance scale score of ≥ 70 points.

Exclusion criteria: (i) distant metastases, (ii) patients who received radiation therapy prior to enrollment in the present study, and (iii) patients who did not provide written informed consent.

Treatment Approach

According to the opinions of the MDT team and the wishes of the patients, 60 patients with locally advanced rectal cancer had the option to be treated with concurrent neoadjuvant chemo-radiotherapy or concurrent postoperative adjuvant chemo-radiotherapy. Of these patients, 27 selected neoadjuvant and 33 selected postoperative concurrent chemo-radiotherapy.

1) Regimen for neoadjuvant chemo-radiotherapy;

Neoadjuvant chemo-radiotherapy: Radiation therapy was performed using pelvic IMRT irradiation at a dose of 45-50.4 Gy/25-28 F/5-6 weeks and concurrent chemotherapy with fluorouracil at a dose of 225 mg/m²/d d1-5 qw. Interval: a 6-8 week period of rest after radiation therapy. Surgery: Surgeoning treatment was performed 6-8 weeks after chemo-radiotherapy. The surgeon determined the specific surgical method.

2) Regimen for postoperative adjuvant chemotherapy;

Surgery: The patient first underwent radical resection of rectal cancer and the surgeon determined the specific surgical method.

Postoperative adjuvant chemotherapy: mFOLFOX6. Oxaliplatin (OXA): 85 mg/m² iv d1; Calcium leucovorin: 400 mg/m² iv d1; and 5-fluorouracil: 400 mg/m² iv bolus d1 and 2400 mg/m² intravenously pumped for 48 hours, d1-2; 14 d/cycle \times 2 cycles.

Concurrent chemo-radiotherapy: IMRT technique pelvic irradiation was used for radiotherapy with a total dose of 45-50.4 Gy/25-28 F/5-6 weeks, and the concurrent chemotherapy regimen was the same as preoperative neoadjuvant chemotherapy.

3) Nutrition and supportive treatment;

The patients received the correct nutritional instructions and the appropriate parenteral nutrition. Patients' sugar, protein and fat requirements were calculated based on their weight, digestive tract symptoms, stress state, etc., and electrolytes and vitamins were supplemented as needed throughout the course of treatment according to individual needs of each patient.

EVALUATION METHODS

Evaluation of nutritional status: Evaluation was carried out weekly using the NRS 2002¹¹ and PG-SGA¹² scales. The NRS 2002 consists of three parts, that is, nutritional status (0-3 points), disease severity (0-3 points) and age (0-1 points). A score of 0 to 2 means that there is no nutritional risk and 3 means that there is nutritional risk that requires nutritional support. The PG-SGA includes seven aspects, that is, weight, food intake, symptoms, activities, and physical functions, the relationship between disease and nutritional needs, metabolic needs, and a physical examination. The first four aspects are self-evaluated by the patient (score A), and the other three aspects are completed by the medical staff (B: disease score, C: stress score, and D: physical examination score). These four scores (A, B, C, and D) are added to get the final score. A score of 0-1 indicates good nutrition, 2-3 suspected malnutrition, 4-8 moderate malnutrition, and ≥ 9 severe malnutrition. **Quality of life evaluation:** Evaluation was carried out using EORTC QLQ-C30 and QLQ-CR38. The 30 items on the QLQ-C30 can be divided into 15 areas including 5 functional areas (physical, role, cognitive, emotional and social functions), 3 symptom areas (fatigue, pain, and nausea and vomiting), 1 overall health status or QOL area, and 6 individual items. The scores of the items included in each field are added together and divided by the number of items included to get the field score. The 38 elements of the QLQ-CR38 are divided into four functional dimensions (body image, sexual function, sexual pleasure, and future expectations) and eight symptom dimensions (urination problems, gastrointestinal symptoms, chemotherapy side effects, defecation problems, stoma problems, male sexual function, female sexual function, and weight). The scores of the items included in each field are added together and divided by the number of items included to get the field score. **Evaluation of acute toxicity:** Toxicity during chemo-radiotherapy was evaluated using the CTC 3.0 standard¹³.

OUTCOME MEASURES

Primary Outcome Measures

The NRS 2002 and PG-SGA nutritional scores before and after concurrent chemo-radiotherapy.

Secondary outcome measures: QOL before and after chemo-radiotherapy (EORTC QLQ-C30 and QLQ-CR38); acute toxicity during chemo-radiotherapy; and incidence rate, time of occurrence, and duration of treatment delays.

OBSERVATIONS AND TIME NODES

The examinations mentioned above were performed weekly during chemotherapy to assess nutritional status, quality of life and toxicity due to chemotherapy of the patients. Specific observations and time nodes are shown in Table I.

STATISTICAL METHODS

We used SPSS 22.0 software (IBM, Chicago, USA) to perform the statistical analysis. Continuous variables were expressed as mean \pm standard deviation. Discrete variables were expressed as percentage. For two-way comparisons, a t test was used for normally distributed data, and the Mann-Whitney U test for nonnormally distributed data. To compare multiple datasets, analysis of variance was used for normally distributed data, and the Kruskal-Wallis test was used for nonnormally distributed data. Discrete data were compared using the chi-square test. $P < 0.05$ was considered statistically significant.

Results

A total of 60 patients with locally advanced rectal cancer who underwent concurrent preoperative or postoperative chemo-radiotherapy in the Department of Abdominal Oncology of the Affiliated Cancer Hospital of Guizhou Medical University from December 2017 to December 2018 were enrolled in this study and their clinical data were collected.

EVALUATION OF NUTRITIONAL RISK

NRS 2002 was used to assess the nutritional risk of the 60 patients with locally advanced rectal cancer before and after chemo-radiotherapy. The results showed that the prevalence of nutritional risk before and after chemo-radiotherapy was 38.33% (23 of 60) and 53% (32 of 60), respectively.

Evaluation of Nutritional Status

Of the 60 patients, 28 in the well-nourished group had PG-SGA scores < 2 before and after concurrent chemo-

TABLE I - Observations and time node of the patients.

Project	Baseline before concurrent chemo-radiotherapy	Weekly during concurrent chemo-radiotherapy	After concurrent chemo-radiotherapy
Blood routine	X	X	X
Blood chemistry	X	–	X
Tumor marker	X	–	X
Film degree exam	X	–	X
Nutritional status score	X	X	X
Quality of Life	X	–	X
Acute toxicity	–	X	X
Treatment termination/delay	–	X	–

Note: X indicates that the item is being carried out, – indicates that the item has not been made.

TABLE II - Trend of nutritional risk of NRS 2002 and nutritional status of PG-SGA in neoadjuvant/postoperative adjuvant concurrent chemo-radiotherapy group.

Time point	Nutritional risk of NRS 2002				Nutritional status of PG-SGA			
	Neoadjuvant concurrent chemo-radiotherapy (27cases)	Postoperative adjuvant concurrent chemo-radiotherapy group (33cases)	Z	P	Neoadjuvant concurrent chemo-radiotherapy (27cases)	Postoperative adjuvant concurrent chemo-radiotherapy group (33cases)	Z	P
Before	1(1,3)	1(1,3)	-0.009	0.993	1(1,2)	1(1,1)	-1.905	0.057
Week 1	2(2,3)	2(2,3)	-0.733	0.463	1(1,2)	1(1,1)	-2.146	0.062
Week 2	2(2,3)	2(2,3)	-0.624	0.533	1(1,2)	1(1,1)	-1.779	0.075
Week 3	2(2,3)	2(2,3)	-0.624	0.533	1(1,2)	1(1,2)	-1.428	0.153
Week 4	3(2,3)	2(2,3)	-0.517	0.605	1(1,2)	1(1,2)	-1.141	0.254
Week 5	3(2,3)	2(2,3)	-0.923	0.356	2(1,3)	1(1,2)	-1.594	0.111
After	3(2,4)	2(2,3)	-1.115	0.265	2(1,3)	2(1,2)	-0.899	0.369

radiotherapy, 15 in the undernourished group had PG-SGA scores <2 before and after concurrent chemo-radiotherapy, the incidence of nutritional deficiencies in patients with locally advanced rectal cancer was 25% (15 of 60), and there were 17 patients in the group that changed nutritional values (PG-SGA score <2 before concurrent chemo-radiotherapy <2 during and after). The PG-SGA scores of the patients in the undernourished group were higher than those of the well-nourished group and the group changed in nutrition during chemo-radiotherapy ($P < 0.05$).

EVALUATION OF NRS 2002 AND PG-SGA AFTER NEOADJUVANT OR POSTOPERATIVE ADJUVANT CHEMO-RADIOTHERAPY

Of the 60 patients, 27 underwent neoadjuvant therapy and 33 underwent concurrent postoperative adjuvant

chemo-radiotherapy. The incidence of nutritional risk and undernutrition was 37% (10 of 27) and 22% (6 of 27), respectively, in the neoadjuvant chemotherapy group and 39.4% (13 of 33) and 27% (9 of 33), respectively, in the postoperative adjuvant chemotherapy group. There were no significant differences in nutritional risk and status between the two groups before and after concurrent chemo-radiotherapy (Table II).

EVALUATION OF QLQ-C30 BEFORE AND AFTER CHEMO-RADIOTHERAPY

A significant difference in the incidence of nausea, vomiting ($p = 0.000$) and diarrhea ($p = 0.045$) was found between the well-nourished, undernourished, and nutrition-changed groups after concurrent chemo-radiotherapy (Table III).

TABLE III - Comparison of QLQ-C30 scale for quality of life before and after treatment among the three groups.

Project	Before treatment					After treatment				
	Good nutr	Under nutr	changed Nutr	χ^2	P	Good nutr	Under nutr	changed Nutr	χ^2	P
Physical function	100(100, 100)	100(100, 100)	100(93, 100)	0.432	0.845	100(100, 100)	100(100, 100)	100(93,100)	0.841	0.657
Role function	100(100, 100)	100(100, 100)	100(100,10)	0.504	0.777	100(100, 100)	100(100, 100)	100(100,10)	1.096	0.578
Emotional function	100(100, 100)	100(100, 100)	100(100,10)	1.053	0.591	100(100, 100)	100(100, 100)	100(100,10)	1.713	0.425
Cognitive function	100(100, 100)	100(100, 100)	100(67, 100)	0.85	0.654	100(100, 100)	100(100, 100)	100(67,100)	0.630	0.730
Social function	100(67, 100)	83(67, 100)	100(75, 100)	1.813	0.404	100(67, 100)	83(67, 100)	100(75,100)	2.103	0.349
tired	0(0,11)	0(0,11)	0(0,11)	1.564	0.516	0(0,11)	0(0,11)	0(0,11)	1.628	0.533
feel sick and vomit	0(0,33)	0(0,33)	0(0,33)	0.946	0.441	0(0,0)	33(33,33)	0(0,0)	12.22	*0.000
pain	-	-	-	-	-	-	-	-	-	-
Shortness of breath	-	-	-	-	-	-	-	-	-	-
insomnia	-	-	-	-	-	-	-	-	-	-
Loss of appetite	-	-	-	-	-	-	-	-	-	-
constipation	-	-	-	-	-	-	-	-	-	-
diarrhea	-	-	-	-	-	0(0,0)	33(33,67)	0(0,0)	8.22	*0.045
Economic difficulties	0(0,33)	0(0,33)	0(0,33)	2.215	0.446	33(0,33)	33(0,33)	33(0,33)	2.316	0.512
Overall quality of life	83(83, 83)	83(67, 83)	83(66,5,100)	3.101	0.212	83(67, 83)	67(67, 83)	83(66, 83)	2.865	0.239

Note: *, $P < 0.05$ was considered statistically significant.

EVALUATION OF QLQ-CR38 BEFORE AND AFTER CHEMO-RADIOTHERAPY

The patients in the well-nourished and nutrition-changed groups cared more about body image before treatment than those of the undernourished group ($P = 0.027$). Patients in the well-nourished group had higher future expectations after receiving concurrent chemo-radiotherapy than patients in the other groups ($P = 0.013$). The patients in the undernourished group had aggravated gastrointestinal symptoms ($P = 0.002$; Table IV).

ACUTE TOXICITY IN PATIENTS DURING CHEMO-RADIOTHERAPY

Neutropenia ($P = 0.006$), nausea and vomiting ($P = 0.000$), diarrhea ($P = 0.000$), and radiation dermatitis ($P = 0.000$) were more severe in the undernourished group than in the well-nourished and nutrition-changed groups during chemo-radiotherapy (Table V). There were no statistically significant differences in acute toxicity between patients receiving neoadjuvant chemo-radiotherapy and concurrent postoperative chemo-radiotherapy (Table VI).

TREATMENT DELAYS

One patient in the well-nourished group (3%), seven in the undernourished group (46%), and two in the nutrition-changed group (11.7%) experienced a delay in treatment. Treatment delays were earlier ($P = 0.015$) and lasted longer ($P = 0.008$) in the undernourished group than in the other two groups. However, there were no significant differences in the incidence of treatment delays between the three groups ($P > 0.05$).

Discussion

The 2016 Guidelines for Colorectal Cancer Nutritional Therapy¹⁴ indicate that rectal cancer can cause malnutrition, which can cause patients to miss the best time for surgery, reduce the effect of chemo-radiotherapy, prolong hospital stay, increase financial burden on patients, and increase complications and mortality. Due to the high incidence of undernutrition in patients with intestinal tumors, nutritional therapy has become an important part of the comprehensive treatment of malignant tumors. The causes of undernutrition include: 1) direct invasion of the digestive tract by the tumor; 2) a large

TABLE IV - Comparison of QLQ-CR38 scale for quality of life before and after treatment among the three groups.

Project	Before treatment					After treatment				
	Good nutr	Under nutr	Changed Nutr	χ^2	P	Good nutr	Under nutr	changed Nutr	χ^2	P
Body image	100 (91.75, 100)	89(78, 100)	100 (100, 100)	7.26	*0.027	100 (89, 100)	89 (78, 100)	100(94.5, 100)	2.482	0.289
Sexual function	100 (71, 100)	100(67, 100)	100(67, 100)	1.079	0.583	100 (67, 100)	83 (67, 100)	100(67, 100)	1.528	0.466
Sexy	100(67, 100)	67(67, 100)	100(75, 100)	2.249	0.325	100 (67, 100)	67 (67, 100)	100(67, 100)	2.16	0.34
Future expectations	83.5 (67, 100)	67(33, 67)	100(67, 100)	4.994	0.082	100 (67, 100)	67 (33, 67)	100(67, 100)	8.722	*0.013
Urination problem	-	-	-	-	-	0(0,0)	0(0,11)	0(0,0)	2.051	0.339
Abdominal symptoms	0(0,0)	0(0,7)	0(0,0)	6.065	0.062	0(0,14)	13(13,13)	0(0,13)	10.017	*0.002
Defecation problem	0(0,14)	10(0,14)	0(0,14)	2.017	0.363	0(0,14)	0(0,14)	0(0,14)	1.208	0.691
Artificial anal problem	0(0,14)	10(5,24)	5(0,10)	0.808	0.891	0(0,14)	0(0,10)	0(0,10)	2.143	0.558
Male sexual dysfunction	-	-	-	-	-	-	-	-	-	-
Female sexual dysfunction	-	-	-	-	-	-	-	-	-	-

Note: *, P<0.05 was considered statistically significant.

TABLE V - Comparison of toxicities of patients in the three groups during chemo-radiotherapy

Project	Groups			χ^2	P
	Good nutr	Under nutr	changed Nutr		
Hemoglobin	2	4	4	1.011	0.603
leukocyte	22	34	31	0.297	0.862
Neutrophil	19	43	19	10.286	*0.006
Platelet	3	0	3	2.011	0.366
liver function	5	7	5	2.812	2.812
Renal function	1	1	2	2.045	2.360
diarrhea	17	50	19	14.396	*0.000
feel sick and vomit	20	70	31	18.377	*0.000
Radiation dermatitis	11	45	27	12.794	*0.000

degree of change in the metabolism of energy, carbohydrates, fats, and protein caused by malignant tumors; 3) the secretion of destructive factors by the tumor that interfere with the digestive function of patients; 4) loss of appetite caused by the tumor; 5) surgery that seriously affects intestinal structure and function; 6) radiotherapy (eg, abdominal pelvic radiotherapy can cause nausea, vomiting, diarrhea, and other gastrointestinal

symptoms that can induce or aggravate malnutrition); 7) chemotherapy can cause gastrointestinal toxicity, which can aggravate the nutritional status of patients.

Nutritional risk refers to the risk that a patient has adverse outcomes due to existing or potential nutrition-related factors¹⁵. Malnutrition includes both undernutrition and obesity. In this study, malnutrition in patients with locally advanced rectal cancer refers to undernutri-

TABLE VI - Comparison of toxicities in the two groups during chemo-radiotherapy (neoadjuvant group/postoperative adjuvant group).

Project	Groups		χ^2	P
	Neoadjuvant concurrent chemo-radiotherapy (27cases)	Postoperative adjuvant concurrent chemo-radiotherapy group (33cases)		
Hemoglobin	6	4	1.483	0.834
leukocyte	36	41	4.011	0.404
Neutrophil	38	43	5.982	0.425
Platelet	3	3	—	—
liver function	6	11	8.510	0.075
Renal function	1	3	2.015	0.354
diarrhea	38	48	9.189	0.074
feel sick and vomit	69	52	7.773	0.086
Radiation dermatitis	37	46	9.872	0.062

Note: *, $P < 0.05$ was considered statistically significant.

tion, which generally refers to protein-energy malnutrition. Globally, the selection of screening and evaluation scales remains a controversial topic^{16,17}. In this study, the NRS 2002 and PG-SGA scales were used for the evaluation of nutritional risk and nutritional status, and we found that patients with nutritional deficiencies also had nutritional risks. Therefore, the two scales present good consistency and fit for our study design. In this study, NRS 2002 was used to assess the nutritional risk and status of patients with locally advanced rectal cancer, and the incidence of nutritional risk was found to be 38.33% (23 of 60), which is consistent with previous studies¹⁸⁻²². We also found that the nutritional risk of patients with locally advanced rectal cancer before, during, and after concurrent chemo-radiotherapy gradually increased (38.33%, 43%, and 53%, respectively; $P < 0.05$). A dynamic evaluation using the PG-SGA scale before, during and after chemo-radiotherapy showed that the incidence of undernutrition in patients with locally advanced rectal cancer was 25% (15 of 60); and some patients were well nourished before treatment, but became undernourished during and after chemo-radiotherapy, suggesting that even if there is no nutritional risk before treatment, patients should be regularly evaluated for nutritional risks and status during and after treatment. Subgroup analysis showed that the incidence of nutritional risk and undernutrition in patients with locally advanced rectal cancer who received concurrent postoperative adjuvant chemotherapy (39.4% and 27%, respectively) was slightly higher than in patients receiving concurrent neoadjuvant chemotherapy (37.0% and 22%, respectively), but the difference was not significant ($P > 0.05$), and there was no significant difference in the trends of nutritional risk and status during and after concurrent chemotherapy between the two groups. In this study, the two above-mentioned scales were used in combination to analyze the quality of life of patients

with locally advanced rectal cancer. The results showed that patients with adequate nutrition had higher future expectations and cared more about their body image than patients in the undernourished group. Patients in the undernourished group had more severe gastrointestinal symptoms such as nausea, vomiting, and diarrhea after chemo-radiotherapy, and their quality of life was worse than that of the well-nourished and nutrition-changed groups.

Patients with locally advanced rectal cancer who were enrolled in this study received preoperative neoadjuvant concurrent chemo-radiotherapy ($n = 27$) and postoperative adjuvant concurrent chemo-radiotherapy ($n = 33$). In terms of acute toxic side effects that occurred during concurrent chemo-radiotherapy in the two groups, the number of cases of diarrhea and radiation dermatitis was slightly higher in the postoperative concurrent chemo-radiotherapy group, but this difference was not statistically significant. This is inconsistent with previous reports²³, in which the toxicity of postoperative concurrent chemo-radiotherapy, especially grade 3/4 acute toxicity, was significantly higher than that of preoperative concurrent neoadjuvant chemo-radiotherapy. The reason was that the pelvic radiotherapy target volume delineation used in the postoperative concurrent chemo-radiotherapy group referred to the consensus on the delineation of the conformal / intensity modulated target volume for rectal cancer developed by the Specialized Committee for Radiation Therapy for Colorectal Neoplasms, Chinese Medical Association²⁴ (the scope of pelvic radiotherapy is appropriately reduced). The incidence of nonhematologic toxicity (nausea, vomiting, diarrhea, and radiation dermatitis) and hematologic toxicity (neutropenia) was higher in patients with nutritional deficiencies than in the nutritionally sufficient and nutrition-changed groups. Although there were no statistically significant differences in the incidence of treatment delay between the three

groups in this study, patients in the undernourished group had an earlier occurrence time and longer duration, indicating that undernourished patients had a significantly reduced tolerance to chemo-radiotherapy. However, this may be related to the small sample size used in this study.

Some scholars have found that the prognostic nutritional index (PNI) and the Naples prognostic score (NPS) are also important parameters to evaluate the nutritional status of patients with gastrointestinal tumors, and found a direct relationship with the prognosis of patients and the incidence of postoperative complications²⁵⁻²⁷. In addition to the above nutritional evaluation indicators, we can add these indicators in the following case collection and long-term follow-up to better evaluate the nutritional status and prognosis of patients.

This study has some limitations. First, it was not a randomized controlled trial. Second, it was only a single center trial and the sample size was limited. Third, the clinical follow-up was short and, in the future, it is necessary to observe the long-term clinical prognosis.

In summary, there is a degree of nutritional risk and deficiencies in patients with locally advanced rectal cancer, and undernourished patients have poorer quality of life and reduced tolerance to chemo-radiotherapy. This provides a clinical basis for improved nutritional interventions and improved quality of life for rectal cancer patients in the future. Routine and continuous nutritional status assessments, nutritional education and nutritional counseling, as well as systematic and standardized intra and extraintestinal nutritional therapy, will be important components of the multidisciplinary approach to the treatment of locally advanced rectal cancer.

Riassunto

Il cancro del retto è una delle neoplasie gastrointestinali più comuni e la maggior parte dei casi include tumori localmente avanzati al momento della diagnosi (stadio II/III).

Lo scopo di questo studio è di osservare i cambiamenti dinamici nello stato nutrizionale dei pazienti con cancro del retto localmente avanzato durante la radioterapia e la chemioterapia concomitanti e di valutare il rischio nutrizionale e l'incidenza della malnutrizione in questi pazienti.

Per questo studio sono stati arruolati un totale di 60 pazienti con cancro del retto localmente avanzato. Per valutare il rischio e lo stato nutrizionale sono stati utilizzati lo screening del rischio nutrizionale e le scale di valutazione globale soggettiva generate dal paziente (PG-SGA) del 2002. Per la valutazione della qualità della vita sono state utilizzate le scale QLQ-C30 e QLQ-CR38 dell'Organizzazione europea per la ricerca e il trattamento del cancro. La tossicità è stata valutata utilizzando lo standard CTC 3.0.

RISULTATI: L'incidenza del rischio nutrizionale tra questi 60 pazienti era del 38,33% (23 su 60) prima e del 53% (32 su 60) dopo la chemio-radioterapia concomitante. Nel gruppo ben nutrito c'erano 28 pazienti, con un punteggio PG-SGA <2 punti, e 17 pazienti nel gruppo con nutrizione modificata, con un punteggio PG-SGA <2 punti prima e 2 punti durante e dopo la chemioradioterapia.

Nel gruppo ben nutrito, l'incidenza di nausea, vomito e diarrea menzionata nel riassunto era inferiore e le aspettative per il futuro (secondo le scale QLQ-CR30 e QLQ-CR28) erano maggiori rispetto al gruppo denutrito. Il gruppo denutrito ha richiesto un trattamento ritardato più spesso e ha manifestato nausea, vomito e diarrea prima e più a lungo rispetto al gruppo ben nutrito. Questi risultati mostrano che la qualità della vita del gruppo ben nutrito era migliore.

In conclusione c'è un grado di rischio nutrizionale e di carenza nei pazienti con cancro del retto localmente avanzato. La chemioradioterapia aumenta l'incidenza del rischio e delle carenze nutrizionali.

References

1. Pressoir M, Desné S, Berchery D, et al: *Prevalence, risk factors and clinical implications of malnutrition in French Comprehensive Cancer Centres*. Br J Cancer, 2010; 102(6):966-71.
2. Pan H, Cai S, Ji J, et al: *The impact of nutritional status, nutritional risk, and nutritional treatment on clinical outcome of 2248 hospitalized cancer patients: A multi-center, prospective cohort study in chinese teaching hospitals*. Nutr Cancer, 2013; 65(1):62-70.
3. Shi YY, Zhang XW, Yuan KT, Xue CL, Yu HL, Shi HP: *Introduction to PG-SGA operating standards. Chinese journal of cancer prevention and treatment introduction to PG SGA operating standards*. Journal of Cancer Treatment, 2013; 20(22):1779-782.
4. Gabrielson DK, Scaffidi D, Leung E, Stoyanoff L, Robinson J, Nisenbaum R, Brezden-Masley C, Darling PB: *Use of an abridged scored patient-generated subjective global assessment (PG-SGA) as a nutritional screening tool for cancer patients in an outpatient setting*. Nutrition & Cancer, 2013; 65(2):234-239.
5. Cotogni P, Pedrazzoli P, De Waele E, Aprile G, Farina G, Stragliotto S, De Lorenzo F, Caccialanza R: *Nutritional therapy in cancer patients receiving chemo-radiotherapy: Should we need stronger recommendations to act for improving outcomes?* J Cancer, 2019; 10(18):4318-325.
6. Yu JC: *Perioperative nutritional support for patients with colorectal cancer*. Chinese Journal of Colorectal Diseases, 2013; 2(2):10-14.
7. Hu WH, Cajas-Monson LC, Eisenstein S, et al: *Preoperative malnutrition assessments as predictors of postoperative mortality and morbidity in colorectal cancer: An analysis of ACS-NSQIP*. Nutr J, 2015; 14:91.
8. Yamano T, Yoshimura M, Kobayashi M, Beppu N, Hamanaka M, Babaya A, Tsukamoto K, Noda M, Matsubara N, Tomita N: *Malnutrition in rectal cancer patients receiving preoperative chemo-*

radiotherapy is common and associated with treatment tolerability and anastomotic leakage. *Int J Colorectal Dis*, 2016; 31(4):877-84.

9. Lin J, Peng J, Qdaisat A, Li L, Chen G, Lu Z, Wu X, Gao Y, Zeng Z, Ding P, Pan Z: *Severe weight loss during preoperative chemo-radiotherapy compromises survival outcome for patients with locally advanced rectal cancer*. *J Cancer Res Clin Oncol*, 2016; 142(12):2551-60.

10. Yamano T, Tomita N, Sato T, Hayakawa K, Kamikonya N, Matoba S, Uki A, Baba H, Oya N, Hasegawa H, Shigematsu N, Hiraoka M, Shimada M, Noda M, Sakai Y, Sato H, Saegusa M, Takeuchi M, Oguchi M, Oya M, Watanabe M: *Influence of chemo-radiotherapy on nutritional status in locally advanced rectal cancer: Prospective multicenter study*. *Nutrition*, 2020; 77:110807.

11. Jens Kondrup, Henrik Højgaard Rasmussen et al: *Nutritional risk screening (NRS 2002): a new method based on an analysis of controlled clinical trials*. *Clin Nutr*, 2003; 22(3):321-36.

12. Bauer J, Capra S, Ferguson M, et al: *Use of the scored patient-generated subjective global assessment (PG-SGA) as a nutrition assessment tool in patients with cancer*. *Eur J Clin Nutr*, 2002; 56(8):779-85.

13. Andy Trotti, A Dimitrios Colevas, et al: *CTCAE v3.0: Development of a comprehensive grading system for the adverse effects of cancer treatment*. *Semin Radiat Oncol*, 2003; 13(3):176-81.

14. Shi Hanping: *Guidelines for nutritional therapy for colorectal cancer*. *Journal of Cancer Metabolism and Nutrition*, 2016; 3(3):164-65, doi: 10.16689/j.cnki.cn11-9349/r.2016.03.008.

15. Gallois C, Artru P, Lièvre A, Auclin E, Lecomte T, Locher C, Marthey L, Zaimi Y, Faroux R, Pernot S, Barret M, Taieb J: *Evaluation of two nutritional scores' association with systemic treatment toxicity and survival in metastatic colorectal cancer: An AGEO prospective multicentre study*. *Eur J Cancer*, 2019; 119:35-43.

16. Arends J, Bachmann P, Baraco V, Barthelemy N, Bertz H, Bozzetti F, Fearon K, Hütterer E, Isenring E, Kaasa S, Krznaric Z, Laird B, Larsson M, Laviano A, Mühlebach S, Muscaritoli M, Oldervoll L, Ravasco P, Solheim T, Strasser F, de van der Schueren M, Preiser JC: *ESPEN guidelines on nutrition in cancer patients*. *Clin Nutr*, 2017; 36(1):11-48.

17. Velasco C, García E, Rodríguez V, et al: *Comparison of four nutritional screening tools to detect nutritional risk in hospitalized patients: A multicentre study*. *Eur J Clin Nutr*, 2011; 65(2):269-74.

18. Lee SY, Jung MR, Kim CH, Kim YJ, Kim HR: *Nutritional risk screening score is an independent predictive factor of anastomotic leakage after rectal cancer surgery*. *Eur J Clin Nutr*, 2018; 72(4):489-95.

19. Milana Sachlova, Ondrej Majekb, Stepan: *Prognostic: Value of scores based on malnutrition or systemic inflammatory response in patients with metastatic or recurrent gastric cancer*. *Nutrition and Cancer*, 2014; 66(8):1362-70.

20. Gioulbasanis I, Georgoulas P, Vlachostergios PJ, Baracos V, Ghosh S, Giannousi Z, Papandreou CN, Mavroudis D, Georgoulas V: *Mini nutritional assessment*.

21. Pan H, Cai S, Ji J, Jiang Z, Liang H, Lin F, Liu X: *The impact of nutritional status, nutritional risk, and nutritional treatment on clinical outcome of 2248 hospitalized cancer patients: A multi-center, prospective cohort study in Chinese teaching hospitals*. *Nutrition & Cancer*, 2013; 65(1):62-70.

22. Hébuterne X, Lemarié E, Michallet M, de Montreuil CB, Schneider SM, Goldwasser F: *Prevalence of malnutrition and current use of nutrition support in patients with cancer*. *J pen Journal of Parenteral & Enteral Nutrition*, 2014; 38(2):196-204.

23. Sauer R, Becker H, Hohenberger W, Rodel C, Wittekind C, Fietkau R, et al: *Preoperative versus postoperative chemo-radiotherapy for rectal cancer*. *N Engl J Med*, 2004; 351(17):1731-40.

24. Tang Y, Jin J, Zhu Y, Liu SX, Yuan XL, Wang WL, Wang XH, Zhang Z, Tian Y, Gao YH, et al: *Consensus and map of pre-operative/postoperative conformal/modulation radiotherapy target area for rectal cancer*. *Chinese Journal of Radiation Oncology*, 2018; 27(3):227-34.

25. Senger AS, Dincer M, Uzun O, et al: *Impact of preoperative prognostic nutritional index levels on morbidity in colorectal cancer surgery*. *Ann Ital Chir*, 2022; 92:97-101.

26. Guldogan CE, Çetinkaya E, Akgul O, et al: *Does the preoperative prognostic nutritional index predict postoperative complications in patients with colorectal cancer who underwent curative resection* *Ann Ital Chir*, 2017; 88:43-47.

27. Galizia G, Auricchio A, de Vita F, et al: *Inflammatory and nutritional status is a predictor of long-term outcome in patients undergoing surgery for gastric cancer. Validation of the Naples prognostic score*. *Ann Ital Chir*, 2019; 90:404-16.