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ABOUT COVER

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WJGO mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal oncology and covering a wide range of topics including liver cell adenoma, gastric neoplasms, appendiceal neoplasms, biliary tract neoplasms, hepatocellular carcinoma, pancreatic carcinoma, cecal neoplasms, colonic neoplasms, colorectal neoplasms, duodenal neoplasms, esophageal neoplasms, gallbladder neoplasms, *etc.*

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Randomized Controlled Trial

Effects of cognitive behavior therapy combined with Baduanjin in patients with colorectal cancer

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Abstract

BACKGROUND

Cancer-related fatigue (CRF) is the most common concomitant symptom in the treatment of colorectal cancer (CRC). Such patients often present with subjective fatigue state accompanied by cognitive dysfunction, which seriously affects the quality of life of patients.

AIM

To explore the effects of cognitive behavior therapy (CBT) combined with Baduanjin exercise on CRF, cognitive impairment, and quality of life in patients with CRC after chemotherapy, and to provide a theoretical basis and practical reference for rehabilitation of CRC after chemotherapy.

METHODS

Fifty-five patients with CRC after radical resection and chemotherapy were randomly divided into either an experimental or a control group. The experimental group received the intervention of CBT combined with exercise intervention for 6 mo, and indicators were observed and measured at baseline, 3 mo, and 6 mo to evaluate the intervention effect.

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RESULTS

Compared with the baseline values, in the experimental group 3 mo after intervention, cognitive function, quality of life score, and P300 amplitude and latency changes were significantly better ($P < 0.01$). Compared with the control group, at 3 mo, the experimental group had significant differences in CRF, P300 amplitude, and quality of life score ($P < 0.05$), as well as significant differences in P300 latency and cognitive function ($P < 0.01$). Compared with the control group, at 6 mo, CRF, P300 amplitude, P300 latency, cognitive function and quality of life score were further improved in the experimental group, with significant differences ($P < 0.01$). The total score of CRF and the scores of each dimension were negatively correlated with quality of life ($P < 0.05$), while the total score of cognitive impairment and the scores of each dimension were positively correlated with quality of life ($P < 0.05$).

CONCLUSION

CBT combined with body-building Baduanjin exercise can improve CRF and cognitive impairment in CRC patients after chemotherapy, and improve their quality of life.

Key Words: Colorectal cancer; Cognitive behavior therapy; Baduanjin exercise; Cancer-related fatigue; Cognitive function; Quality of life

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Core Tip: Cognitive behavior therapy combined with body-building Baduanjin exercise can improve cancer-induced fatigue and cognitive impairment in colorectal cancer patients after chemotherapy, and improve their quality of life. The quality of life of colorectal cancer patients may be related to cancer-induced fatigue and cognitive level. Cognitive behavior therapy combined with exercise intervention deserves to be promoted in cancer patients.

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INTRODUCTION

Colorectal cancer (CRC) is one of the most common malignancies. According to the 2018 global cancer statistics, the global mortality rate of CRC accounted for 9.2% of the total number of cancer deaths, and the incidence rate accounted for 10.2% of the total number of cancers, ranking second and third, respectively[1]. CRC is mainly treated by surgical resection, combined with perioperative radiotherapy and chemotherapy and other comprehensive treatment methods. Cancer-related fatigue (CRF) is a subjective fatigue state caused by the adverse effects of cancer itself and chemotherapy, and is also affected by social objective factors and individual factors[2]. Cancer-related cognitive impairment (CRCI) is caused by chemotherapy in cancer patients, often referred to as chemotherapy brain or chemotherapy fog[3]. Due to chronic inactivity and the effects of CRF, cancer patients often develop cognitive impairments that ultimately affect their quality of life.

Cognitive behavioral therapy is concerned about the relationship between thought, feeling, and behavior; the main purpose is to reduce stress, in a rational way to solve the patients' severe psychological stress response, so that it can adapt to the changes brought by psychological stress[4]. Exercise therapy as a nondrug method has been pursued by clinicians in recent years. Aerobic exercise can improve the physical status of cancer patients, negative emotions such as anxiety and depression, and cognitive impairment and reduce the level of CRF[5]. Baduanjin is a medium-intensity aerobic exercise that has a good promoting effect on human digestion, respiration, circulation,

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and motor function[6]. So far, there have been few studies on the effect of cognitive behavior therapy (CBT) combined with exercise on cognitive function in patient with CRC. The present study used CBT combined with Baduanjin as the intervention for 6 mo in patients with CRC chemotherapy to explore the value of the combination therapy in the rehabilitation of CRC during chemotherapy.

MATERIALS AND METHODS

Inclusion and exclusion criteria

We recruited patients undergoing chemotherapy for CRC who were admitted to Liaoning Tumor Hospital between March and October 2018. The inclusion criteria were: (1) Subjects met the guidelines for diagnosis, staging, and treatment of CRC[7], and underwent surgery for CRC; (2) In the stable period after surgery (clinical stages I-III); (3) The score of the simple mini-mental state examination scale was 22-27 points; and (4) All patients with CRC successfully completed standardized chemotherapy regimen. The exclusion criteria were: (1) Complicated with serious cardiovascular and cerebrovascular diseases and mental diseases; (2) Presence of limb dysfunction; (3) Accompanied by pneumonia, asthma, and other respiratory diseases; and (4) Had participated in regular exercise during the past 6 mo. This study was approved by the Ethics Committee of Liaoning Tumor Hospital. All subjects participated voluntarily and gave signed informed consent.

Using a random number table method, 60 patients were randomly divided into either an experimental or a control group, with 30 cases in each group. During the study, a total of five patients withdrew from the study, including three in the experimental group who did not complete the treatment on time ($n = 2$) or whose condition deteriorated ($n = 1$), and two in the control group who were readmitted to the hospital for chemotherapy and withdrew from the study. Finally, 27 patients in the experimental group and 28 in the control group completed the study. There was no significant difference in patients' general baseline data or disease-related data between the two groups ($P > 0.05$; Table 1).

Intervention plan

The experimental group received CBT from psychotherapists. The patients provided details of their symptoms and illness for 1 h, three times a week. Doctors provided immediate monitoring and cognitive correction, stress management, cognitive restructuring, and relaxation counseling, and encouraged patients to adopt positive behavioral strategies. After discharge, doctors conducted home visits or telephone communication once a week and completed CBT for 6 mo.

During hospitalization, the experimental group received comprehensive and systematic guidance from professional coaches on the skills and exercise load of Baduanjin, until they could all regulate and master the exercise movements. The videos of Baduanjin were released upon discharge. After discharge, the patients were given weekly telephone supervision and follow-up visits. The patients were asked to write a daily exercise diary. The mean duration of exercise was ≥ 4 d/wk, ≥ 20 d/mo, 45-60 min/session, twice daily (once in the morning and once in the afternoon) for 6 mo. There was no exercise intervention in the control group.

Indicator testing and data processing

The cognitive potential P300 test and scale were evaluated at baseline, and 3 mo and 6 mo after intervention. The changes in cognitive function, CRF, and quality of life of subjects before and after intervention were compared and analyzed, and the effect of intervention was evaluated.

Cognitive function assessment

Functional assessment of cancer therapy-cognitive function (FACT-Cog)[8] comprises 37 items in four dimensions, including correction of cognitive impairment, cognitive ability, evaluation by others, and impact on quality of life; each item has a score of 0-4, with 5 grades. The lower the score, the worse the cognitive function, and the test has good reliability and validity[9].

Assessment of CRF

The Cancer Fatigue Scale (CFS) compiled by Okuyama *et al*[10] was designed for evaluating fatigue symptoms of cancer patients, consisting of 15 items and three

Table 1 Comparison of general information between the two groups of patients, *n* (%)

	Experimental group (<i>n</i> = 27)	Control group (<i>n</i> = 28)	<i>P</i> value
Mean age (range, yr)	52 (44-60)	51 (40-62)	0.516
Gender			
Male	19 (70.4)	21 (75)	0.70
Female	8 (29.6)	7 (25)	
Years of education			
< 9	8 (29.6)	9 (32.2)	0.747
9-12	15 (55.6)	13 (46.4)	
> 12	4 (14.8)	6 (21.4)	
Marital status			
Married	20 (74.1)	24 (85.7)	0.555
Unmarried	2 (7.4)	1 (3.6)	
Divorced	5 (18.5)	3 (10.7)	
Clinical stage			
I	3 (11.1)	2 (7.2)	0.763
II	11 (40.8)	10 (35.7)	
III	13 (48.1)	16 (57.1)	
Chemotherapy			
XELOX	12 (44.4)	10 (35.7)	0.509
FOLOX	15 (55.6)	18 (64.3)	
Mean BMI (kg/m ²)	22.56 (20.38-24.05)	22.71 (21.22-24.19)	0.561
Mean MMSE score	24 (22-27)	24 (22-27)	0.765

XELOX: Capecitabine combined with oxaliplatin; FOLOX: Oxaliplatin combined with calcium folinate and deoxyfluoruridine; BMI: Body mass index; MMSE: Mini-mental State Examination.

dimensions of physical fatigue, emotional fatigue, and cognitive fatigue. Each item was rated on a scale of 1–5, with higher scores indicating more fatigue[11]. Studies have shown that the coefficient of Cronbach's (α) in the total table is 0.84–0.88, and the sub-half reliability coefficient (r) is 0.32–0.67[12].

Quality of life assessment

Functional assessment of cancer therapy-colorectal (FACT-C) is specifically used in the assessment of CRC patients. It consists of generic and CRC-specific modules with five dimensions: Physiological status, social/family status, emotional status, functional status, and additional concern for CRC. The internal consistency coefficient of additional concern was 0.56, the retest correlation coefficient of other fields was ≥ 0.76 , and the α coefficient of all fields and general modules was ≥ 0.80 [13].

Cognitive P300 test

The amplitudes and latency of P300 were recorded using the 32-channel electroencephalography acquisition system produced by Neuroscan Corporation (Charlotte, NC, United States), and the position of electrode was recorded at CZ point, which is located in the central midline of the brain and is the most commonly used electrode placement for recording cognitive-related potentials in the International Electroencephalogram Society 10-20 standard. The test was completed in the Department of Neurology in hospital.

Statistical analysis

SPSS 20.0 was used for data analyses. Quantitative data are expressed as the mean \pm SD. Repeatability measurement analysis of variance was used between groups and

within groups, and Pearson correlation analysis was conducted between variables. Stepwise multiple linear regression was conducted for the variables with high correlation, and $P < 0.05$ was considered significant, and $P < 0.01$ was considered highly significant.

RESULTS

Overall status of all subjects in chemotherapy phase of CRC at baseline

The quality of life, cognitive function, and CRF status of all subjects at baseline are shown in Table 2. Among all the quality of life dimensions, social/family status score was the highest, followed by emotional status, additional concern, physiological status, and functional status (Table 2). Among the cognitive status dimensions, others' evaluation score was the highest, followed by corrected cognitive impairment, cognitive ability, and impact on quality of life. The scores for CRF showed that the scores of each dimension from high to low were physical fatigue, emotional fatigue, and cognitive fatigue.

Changes in CRF before and after intervention

The total score for the CRF test and the scores of each dimension in each group before and after exercise intervention are shown in Figure 1 and Table 3. At baseline, there were no significant differences between the two groups in terms of overall fatigue and each dimension ($P > 0.05$). Compared with baseline values, there were significant differences in the total score ($P < 0.001$), body fatigue score ($P < 0.001$), emotional fatigue score ($P < 0.001$), and cognitive fatigue ($P = 0.013$) in the experimental group at 3 mo and 6 mo after intervention. Compared with the control group, there were significant differences in the total score ($P = 0.018$), body fatigue score ($P = 0.003$), emotional fatigue score ($P = 0.029$), and cognitive fatigue ($P = 0.022$) at 3 mo and 6 mo after exercise intervention in the experimental group ($P < 0.001$).

Changes in cognitive function in the two groups before and after intervention

Status of electrophysiological tests: Figure 2 shows the cognitive potential P300 test of each group before and after exercise intervention. At baseline, there was no significant difference in the latency or amplitude of P300 between the two groups ($P > 0.05$). Compared with baseline values, there were significant differences in latent period ($P < 0.001$) and amplitude of P300 ($P = 0.008$) in the experimental group at 3 mo; furthermore, after 6 mo of intervention, there were highly significant differences in latency and amplitude of P300 ($P < 0.001$). Compared with the control group, there were significant differences in latent period ($P = 0.002$) and amplitude of P300 ($P = 0.041$) at 3 mo; and after 6 mo of intervention, the latency of P300 in the experimental group was shortened and the amplitude of P300 increased, with highly significant differences ($P < 0.001$).

Cognitive scale scores: Figure 3A and Table 4 show the total score of cognitive function and scores of each dimension in each group before and after exercise intervention. At baseline, there were no significant differences between the two groups in FACT-Cog total score or the scores of the four dimensions ($P > 0.05$). Compared with baseline values, 3 mo after intervention, except for impact on quality of life ($P = 0.526$) and other's evaluation ($P = 0.013$), the P values of total FACT-Cog score and the scores of other two dimensions were all less than 0.001; 6 mo after intervention, the P values of total FACT-Cog score and the scores of the four dimensions were all less than 0.001. Compared with the control group, after 3 mo of intervention, there were significant differences in the total score ($P = 0.016$) and scores of corrected cognitive impairment ($P = 0.003$), cognitive ability ($P = 0.011$), and impact on quality of life ($P = 0.002$); after 6 mo of intervention, there were highly significant differences in the total score ($P = 0.002$) and scores of corrected cognitive impairment ($P < 0.001$), cognitive ability ($P = 0.002$), other's evaluation ($P = 0.002$), and impact on quality of life ($P < 0.001$).

Changes in quality of life in the two groups before and after intervention

The total score of quality of life and the scores of the five dimensions in each group before and after exercise intervention are shown in Figure 3B and Table 5. At baseline, there were no significant differences between the two groups in the total score of quality of life or the scores of the five dimensions ($P > 0.05$). Compared with baseline values, 3 mo after intervention, there were significant differences in total score ($P <$

Table 2 Quality of life, cognitive function, and cancer-related fatigue scores at baseline (*n* = 55)

Item	Scale score range	Actual score range	Actual score	Score percentage (%)
Quality of life				
FACT-C total score	0-144	36-131	81.65 ± 23.27	56.72
Physiological status	0-28	6-25	15.38 ± 4.47	54.93
Social/family status	0-28	9-28	19.05 ± 4.57	68.04
Emotional status	0-24	6-24	14.93 ± 4.08	62.21
Functional status	0-28	5-26	12.69 ± 4.46	45.32
Additional attention score	0-36	10-30	19.84 ± 4.87	55.11
Cognitive function				
FACT-Cog total score	38-132	47-108	80.15 ± 10.97	60.72
Corrected cognitive impairment	18-72	26-57	46.62 ± 4.98	64.75
Cognitive ability	0-28	7-22	14.76 ± 3.21	52.14
Other's evaluation	4-16	5-16	10.51 ± 2.28	65.69
Impact on quality of life	4-16	4-13	8.25 ± 2.08	51.75
CRF				
CFS total score	0-60	22-46	34.47 ± 6.59	57.45
Physical fatigue	0-28	11-28	18.09 ± 3.23	64.61
Emotional fatigue	0-16	6-15	8.85 ± 1.82	55.31
Cognitive fatigue	0-16	3-12	7.53 ± 2.05	47.06

FACT-C: Functional assessment of cancer therapy - colorectal; FACT-Cog: Functional assessment of cancer therapy-cognitive function; CRF: Cancer-related fatigue; CFS: Cancer fatigue scale.

Table 3 Comparison of cancer-related fatigue tests in different dimensions (mean ± SD)

Group	Physical fatigue	Emotional fatigue	Cognitive fatigue
Experimental group (<i>n</i> = 27)			
Baseline	17.56 ± 3.53	8.67 ± 1.78	7.37 ± 2.09
3 mo	15.78 ± 2.85 ^{b,e}	7.59 ± 1.67 ^{b,d}	6.59 ± 1.65 ^{a,d}
6 mo	15.19 ± 2.66 ^{b,e}	6.59 ± 1.47 ^{b,c,e}	6.33 ± 1.66 ^{b,e}
Control group (<i>n</i> = 28)			
Baseline	18.61 ± 2.82	9.04 ± 1.80	7.57 ± 2.06
3 mo	18.43 ± 3.71	8.61 ± 1.69	7.79 ± 2.08
6 mo	18.46 ± 3.31	8.68 ± 1.91	7.68 ± 1.83

Intra-group comparison before and after intervention:

^a*P* < 0.05.

^b*P* < 0.01 *vs* baseline.

^c*P* < 0.01 *vs* 3 mo.

Comparison between experimental group and control group at different time:

^d*P* < 0.05.

^e*P* < 0.01, experimental group *vs* control group at baseline/3 mo/6 mo.

0.001), and scores of physiological status (*P* < 0.001), emotional status (*P* < 0.001), and additional attention (*P* = 0.044), while there were no significant differences in the score of social/family status (*P* = 0.455) or functional status (*P* = 0.059); 6 mo after intervention, there were significant differences in total score and the scores of the five dimensions (*P* < 0.001). Compared with the control group, after 3 mo of intervention,

Table 4 Comparison of cognitive function tests in different dimensions (mean \pm SD)

Group	Corrected cognitive impairment	Cognitive ability	Others' evaluation	Impact on quality of life
Experimental group (<i>n</i> = 27)				
Baseline	47.19 \pm 4.14	14.96 \pm 3.47	10.93 \pm 2.24	8.81 \pm 2.08
3 mo	50.26 \pm 3.96 ^{b,e}	17.11 \pm 3.64 ^{b,d}	11.26 \pm 2.33 ^a	9.37 \pm 2.66 ^e
6 mo	54.22 \pm 6.80 ^{b,c,e}	18.30 \pm 4.26 ^{b,c,e}	12.22 \pm 2.28 ^{b,c,e}	10.81 \pm 2.73 ^{b,c,e}
Control group (<i>n</i> = 28)				
Baseline	46.07 \pm 5.73	14.57 \pm 2.87	10.11 \pm 2.25	7.71 \pm 1.94
3 mo	46.21 \pm 5.37	14.68 \pm 3.22	10.14 \pm 2.17	7.32 \pm 2.02
6 mo	46.25 \pm 6.92	14.86 \pm 3.50	10.21 \pm 2.35	7.43 \pm 2.01

Intra-group comparison before and after intervention:

^a*P* < 0.05.

^b*P* < 0.01 *vs* baseline.

^c*P* < 0.01 *vs* 3 mo.

Comparison between experimental group and control group at different time:

^d*P* < 0.05.

^e*P* < 0.01, experimental group *vs* control group at baseline/3 mo/6 mo.

Table 5 Comparison of quality of life tests in different dimensions (mean \pm SD)

Group	Physiological status	Social/family status	Emotional status	Functional status	Additional attention score
Experimental group (<i>n</i> = 27)					
Baseline	16.19 \pm 3.48	19.85 \pm 4.92	15.41 \pm 4.41	13.78 \pm 4.29	11.54 \pm 4.36
3 mo	17.67 \pm 3.96 ^{b,d}	20.59 \pm 4.73 ^d	17.11 \pm 4.47 ^{b,d}	14.74 \pm 4.78 ^e	22.41 \pm 6.08 ^{a,d}
6 mo	18.70 \pm 4.15 ^{b,e}	21.48 \pm 4.57 ^{b,c,e}	17.48 \pm 4.64 ^{b,d}	16.00 \pm 4.84 ^{b,c,e}	24.85 \pm 6.56 ^{b,c,e}
Control group (<i>n</i> = 28)					
Baseline	14.61 \pm 5.18	18.29 \pm 4.14	14.46 \pm 3.76	11.64 \pm 4.44	19.14 \pm 4.28
3 mo	14.89 \pm 5.72	17.75 \pm 4.40	14.32 \pm 3.49	11.32 \pm 4.28	18.71 \pm 5.61
6 mo	14.25 \pm 5.29	18.14 \pm 4.61	14.46 \pm 3.75	11.54 \pm 4.36	19.11 \pm 5.63

Intra-group comparison before and after intervention:

^a*P* < 0.05.

^b*P* < 0.01 *vs* baseline.

^c*P* < 0.01 *vs* 3 mo.

Comparison between experimental group and control group at different time:

^d*P* < 0.05.

^e*P* < 0.01, experimental group *vs* control group at baseline/3 mo/6 mo.

there were significant differences in total score (*P* = 0.016) and the scores of physiological status (*P* = 0.039), social/family status (*P* = 0.025), emotional status (*P* = 0.012), functional status (*P* = 0.007), and additional attention (*P* = 0.023); after 6 mo of intervention, there were highly significant differences in total score (*P* = 0.002) and the scores of physiological status (*P* = 0.001), social/family status (*P* = 0.009), emotional status (*P* = 0.010), functional status (*P* = 0.001), and additional attention (*P* = 0.001).

Relationship between quality of life and CRF and cognitive function in the experimental group before and after intervention

Correlation between quality of life and CRF and cognitive function in the experimental group: Pearson correlation analysis was performed between the total scores of FACT-C and CFS and its three dimensions, and the total score of FACT-Cog and its four dimensions. As shown in Table 6, the total score of quality of life was negatively correlated with the total score of fatigue and the scores of the three dimensions, and the total score of quality of life and cognitive function was positively correlated with

Table 6 Correlation analysis between quality of life and cancer-related fatigue and cognitive dysfunction in experimental group

Item	FACT-C total score	
	<i>r</i>	<i>P</i> value
CFS total score	-0.733	< 0.000
Physical fatigue	-0.439	0.023
Emotional fatigue	-0.487	0.011
Cognitive fatigue	-0.642	< 0.000
FACT-Cog total score	0.753	< 0.000
Corrected cognitive impairment	0.663	< 0.000
Cognitive ability	0.624	0.001
Other's evaluation	0.186	0.342
Impact on quality of life	0.40	0.023

FACT-C: Functional assessment of cancer therapy - colorectal; FACT-Cog: Functional assessment of cancer therapy-cognitive function; CFS: Cancer fatigue scale.

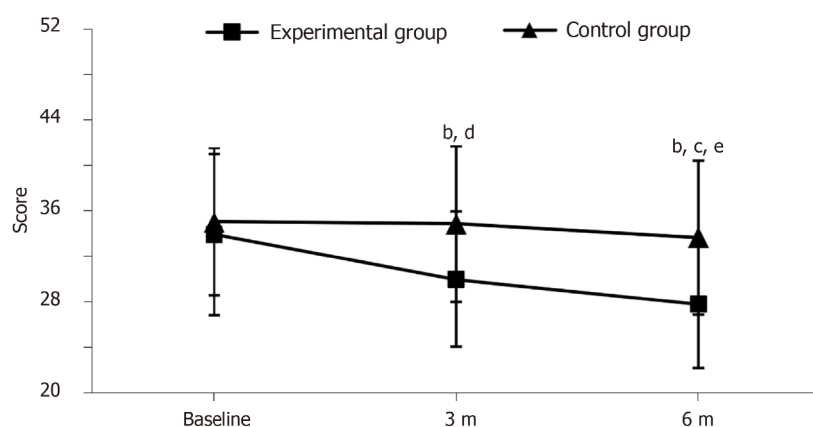


Figure 1 Total Cancer Fatigue Scale scores before and after intervention. Intra-group comparison before and after intervention: ^b*P* < 0.01 vs baseline; ^c*P* < 0.01 vs 3 mo. Comparison between experimental group and control group at different time points: ^d*P* < 0.05, ^e*P* < 0.01, experimental group vs control group at baseline/3 mo/6 mo.

the four dimensions.

Multivariate stepwise regression analysis of quality of life, CRF, and cognitive function in the experimental group: To analyze the relationship between quality of life and CRF and cognitive function, the difference between the total score of quality of life of patients undergoing CRC chemotherapy in the experimental group at 6 mo and the baseline data was used as the dependent variable. Five significant factors in the correlation analysis were taken as independent variables, and the five factors in the multivariate stepwise regression analysis were as follows: CRF total score, cognitive fatigue, FACT-Cog total score, corrected cognitive impairment, and cognitive ability.

The complex correlation coefficient $r = 0.80$ and the adjusted $R^2 = 0.603$ indicated that the dependent variable (total score of quality of life) of the stepwise fitting multiple linear regression equation could be explained by the independent variables (fatigue and cognition) by 60.3%. According to the standard regression coefficient, Table 7 shows that the factors affecting the quality of life of patients with CRC chemotherapy included total score of CRF and total score of FACT-Cog. Linear regression equation can be established according to the following model, with X_1 representing the total score of CRF and X_2 representing the total score of FACT-Cog: $Y = 4.923 - 0.585 X_1 + 0.375 X_2$, the results showed that the CRF score has a greater impact on quality of life than FACT-Cog score. The collinearity diagnosis results showed that all variables had a variance inflation factor (VIF) < 10, and there was no collinearity; therefore, it is of practical significance to establish the corresponding linear regression

Table 7 Stepwise regression analysis results of quality of life scores

Variable	Regression coefficient	SE	Standard regression coefficient	t	P value	Collinearity Statistics	
						Tolerance	VIF
Constant	4.923	1.429		3.209	0.004		
FACT-Cog Total score	0.375	0.149	0.464	2.512	0.019	0.447	2.235
CRF total score	-0.585	0.278	-0.388	-2.103	0.046	0.651	1.535

FACT-Cog: Functional assessment of cancer therapy-cognitive function; CRF: Cancer-related fatigue.

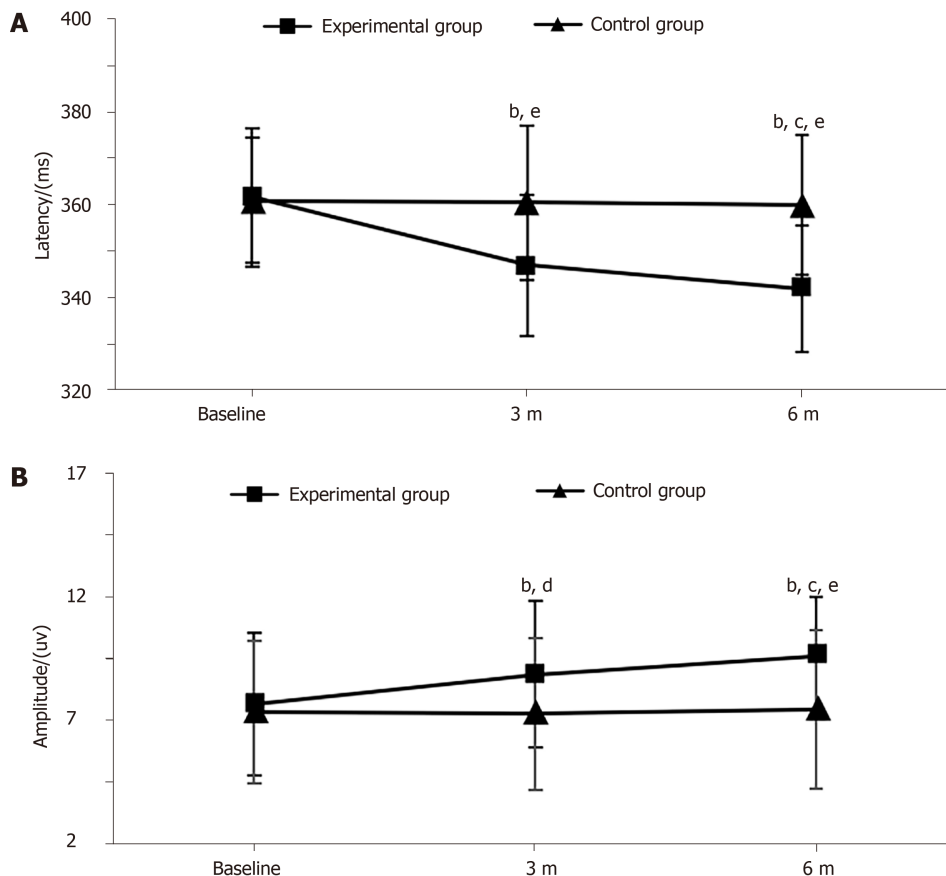


Figure 2 P300 latency and amplitude changes. A: P300 latency change; B: P300 amplitude change. Intra-group comparison before and after intervention: ^b $P < 0.01$ vs baseline; ^c $P < 0.01$ vs 3 mo. Comparison between experimental group and control group at different time points: ^d $P < 0.05$, ^e $P < 0.01$, experimental group vs control group at baseline/3 mo/6 mo.

model. VIF is a common measure for judging the severity of multicollinearity in multiple linear regression models. Usually, 10 is taken as the judgment boundary. When $VIF < 10$, there is no multicollinearity.

DISCUSSION

CRC has high clinical morbidity. With improvement in medical understanding, its fatality rate has decreased year by year. In recent years, people's health awareness has been gradually enhanced, but due to the neglect of early screening of CRC, often the best time for diagnosis and treatment is missed, resulting in adverse effects on recovery[14]. Patients with CRC generally need chemotherapy to inhibit the growth of cancer cells, and most patients with chemotherapy are accompanied by CRF. In addition to less exercise, bed rest, chemotherapy, and other internal and external factors, patients often appear with anxiety, depression, and other negative emotions and varying degrees of cognitive impairment. If the above factors are not effectively

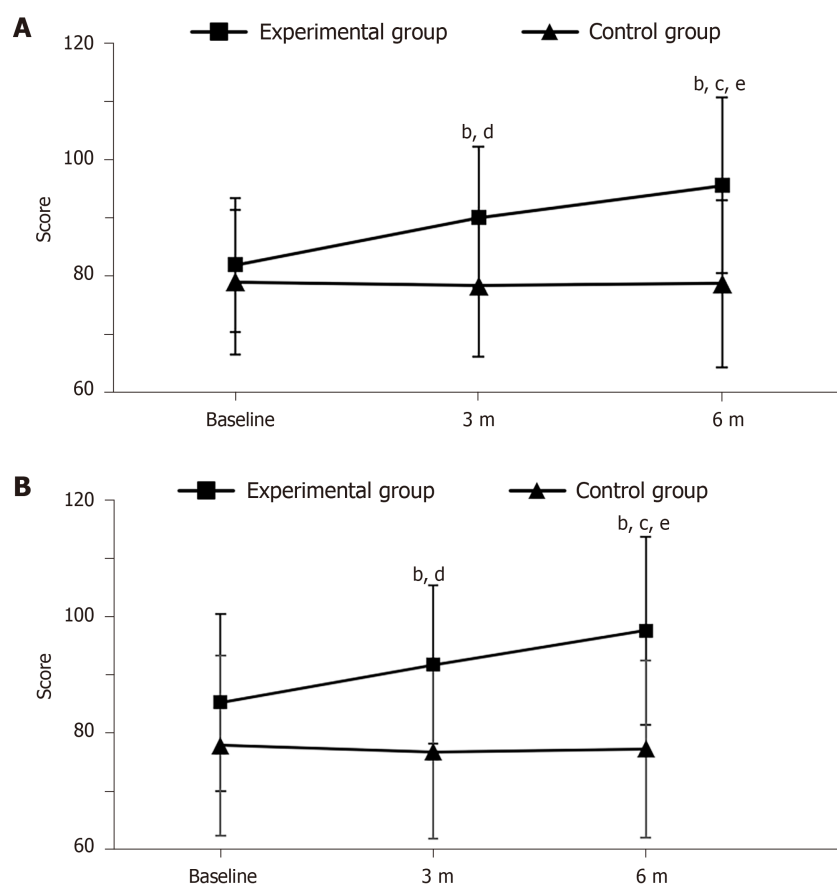


Figure 3 Functional assessment of cancer therapy. A: Functional assessment of cancer therapy-cognitive function total score change before and after intervention. Intra-group comparison before and after intervention: ^b $P < 0.01$ vs baseline; ^c $P < 0.01$ vs 3 mo. Comparison between experimental group and control group at different time: ^d $P < 0.01$, experimental group vs control group at baseline/ 3 mo/ 6 mo; B: Functional assessment of cancer therapy – colorectal total score changes before and after intervention. Intra-group comparison before and after intervention: ^b $P < 0.01$ vs baseline; ^c $P < 0.01$ vs 3 mo. Comparison between experimental group and control group at different time: ^d $P < 0.05$, ^e $P < 0.01$, experimental group vs control group at baseline/ 3 mo/ 6 mo.

resolved or controlled, the cognitive level and quality of life of patients continue to decline, and even aggravate the condition of the patients, forming a vicious cycle. Studies have shown that exercise and psychological intervention could promote the improvement of quality of life in cancer patients[15], and exercise combined with psychotherapy may be an effective intervention to improve CRF in patients with CRC undergoing chemotherapy.

CBT focuses on the relationships between thought, feeling, and behavior, with the goal of reducing stress and fatigue, thereby improving the quality of life of patients. Fitness Qigong Baduanjin, a Chinese traditional Qigong exercise that focuses on a mind-body integration, is considered to be an effective exercise in promoting health. Numerous studies have shown that Baduanjin exercise could effectively relieve physical pain, improve physical function, relieve negative emotions such as anxiety and depression, and have a very good effect on the improvement of cognitive function. It is an effective adjunctive rehabilitation method for cognitive and psychological diseases, and is widely used in clinical practice[16]. A randomized controlled trial has shown that CBT combined with exercise can improve fatigue, sleep disturbance, anxiety, and depression in breast cancer patients[17].

Studies have shown that CRF is a common symptom in about 70% of cancer patients [18]. Fatigue in patients is often more serious than that in healthy groups, and is difficult to alleviate through sleep and rest, causing a major economic burden and mental pressure on patients and their families[19]. At present, there are many studies on the pathogenesis of CRF, among which, the explanation of CRF by 5-hydroxytryptamine (5-HT) disorder has been accepted by most researchers. This mechanism can be divided into two types of CRF: Peripheral and central fatigue[20]. Peripheral fatigue mainly refers to physical fatigue. After cancer patients receive chemotherapy, peripheral nerves can be stimulated to release neuroactive substances, and the vagus afferent nerve can be activated, thus inhibiting skeletal muscle activity. Decrease of skeletal muscle activity leads to physical fatigue. Central fatigue, including emotional

and cognitive fatigue, is mainly related to neural bundles and disorders in the brain, especially the increased concentration of 5-HT in the brain[21]. In the present study, the CFS was used to evaluate the degree of CRF, and it was found that body fatigue was most severe in patients undergoing chemotherapy for CRC, and this conclusion is consistent with the research of Jong *et al*[22]. Studies have confirmed that moderate physical activity has a good effect in improving CRF in patients with CRC, but most of the aerobic exercises used in existing studies are jogging, swimming, cycling, *etc.*, and the efficacy evaluation also focuses on a single time point and lacks periodic efficacy observation. In this study, Chinese traditional healthy Qigong Baduanjin was used to intervene patients with CRC for 6 mo, and the CFS was evaluated at 3 and 6 mo. The results showed that exercise intervention for 3 mo could improve the CRF of CRC patients significantly, among which the improvement of body fatigue was the most obvious, and still had a certain curative effect with the extension of intervention time. Therefore, Baduanjin is a good exercise intervention method for CRF, which is worthy of long-term adherence.

Cancer patients often have cognitive impairment, mainly for memory, attention, and event processing speed[23]. This may be caused by effects of chemotherapeutic drugs on the CNS and nerve cell damage directly, resulting in oxidative stress, inflammatory reaction, and changes in hormone levels, blood supply, and metabolism[24]. However, it should be noted that mild cognitive impairment is not easily detected by the patients themselves, and their families often focus on the recovery of disease symptoms, while the symptoms of CRCI, such as decline in memory and attention, are easily ignored. In this study, the FACT-Cog scale was used to evaluate the cognitive function of CRC patients from multiple dimensions, which showed that, there are different degrees of cognitive impairment in CRC patients; among the dimensions of the scale, the lowest score was for impact on quality of life and cognitive ability, while the highest score was for other people's evaluation. The reason may be that the cognitive impairment caused by chemotherapy for CRC makes the patients unable to have normal work and social skills, and affect the quality of life ultimately. Studies have shown that physical activities can improve cognitive function in patients, which may be because exercise stimulates the cranial nerves, activates the CNS, prevents brain atrophy, and increases the hippocampal volume, thereby promoting the remodeling of nerve cells and synapses[25]. Furthermore, Ferguson *et al*[26] found that CBT therapy could improve cognitive dysfunction and the quality of life effectively in breast cancer survivors following chemotherapy. In the present study, after 6 mo of Baduanjin and CBT intervention, the five main dimensions of FACT-Cog scale were improved significantly, and the results are consistent with those of previous studies. To further analyze the effect on the cognitive function of CRC patients, we used P300, which provides objective evidence for the theory that CBT combined with exercise intervention can improve related cognitive dysfunction in patients with CRC chemotherapy. P300 is an effective electrophysiological indicator reflecting cognitive function status. The latency of P300 is often used to reflect short-term memory, selective attention, and reaction speed, the ability to process events, and cognitive processing[27], and the amplitude of P300 reflects the resources invested in the brain when it senses incoming stimulus information, namely, the active control of attention and the ability of information processing. The decrease of P300 amplitude and the prolongation of latency indicate the decline of cognitive ability, and P300 latency is more sensitive to the occurrence of early CRCI than P300 amplitude response, so P300 amplitude and latency can be used as biological markers of cognitive physiological mechanism[28,29]. The present study was completed by auditory stimulation under the oddball paradigm, and the latency of P300 was significantly shortened and the amplitude of P300 was significantly increased in CRC patients receiving 3 mo of CBT combined with exercise intervention, and the difference became more significant with the duration of the intervention. In addition, the above changes were not observed in the control group, which was consistent with the scale evaluation results, confirming the effectiveness of combined intervention for CRCI in this type of disease.

In recent years, the quality of life of patients with CRC during chemotherapy has attracted much attention. Different from the traditional biomedical models, modern medical models do not take tumor elimination as the only goal, and their evaluation of survival rate of cancer patients is more systematic, especially paying attention to the quality of life of patients after surgery and chemotherapy[30]. The concept of quality of life is extremely complex, including physical, psychological, social function, mental state, *etc.* It reflects the gap between personal expectations and actual living conditions. Research has shown that CRC surgery and chemotherapy cause changes in normal defecation patterns and disorder of self-image, and lead to negative emotions such as anxiety and depression, and then affect the quality of life of patients seriously[31]. In

this study, the FACT-C scale was used to evaluate the quality of life of patients with CRC after chemotherapy, and then we found a general decline in quality of life. For the FACT-C scale, the decline of functional status is the most obvious, followed by physiological status and additional attention score, and the decline of social/family status is relatively small. The reason may be that after cancer chemotherapy, patients get the support and encouragement from family and friends, and get a great emotional release. Physical activities are closely related to the quality of life of CRC patients. A large number of studies have shown that the overall quality of life of patients who participate in physical activities for a long time is significantly higher than that of patients who do not [32]. Baduanjin exercise has been found effective in improving the quality of life and mental health, and reducing stress [33]. Ferguson *et al* [26] also found that 2 mo of brief cognitive-behavioral therapy intervention could improve the quality of life and verbal memory performance of breast cancer survivors effectively. In this study, we found that the scores of the four dimensions of the FACT-C scale were improved after 3 mo of Baduanjin combined CBT intervention in patients with CRC after chemotherapy, and the quality of life was further improved by 6 mo of intervention. Baduanjin exercise could improve the physical function and CBT could relieve the negative emotion effectively, and they cooperate with each other and play a benign promoting role together.

In this study, we analyzed the correlation between quality of life and CRF and cognitive function in patients undergoing chemotherapy for CRC, and found that patients with more severe CRF had lower quality of life. CRF causes many problems for cancer patients, including daily diet, daily life, leisure and entertainment, normal working ability, *etc.* The total score of cognitive function and the scores of each dimension are closely related to the total score of quality of life. The reason may be that chemotherapy and other factors lead to the cognitive decline. Cancer patients are often unable to concentrate and their memory declines, which seriously affects their normal social activities. Therefore, it will also have an impact on the quality of life of patients. In our study, the decrease in quality of life of subjects was mainly related to CRF, followed by CRCI. CRF and CRCI caused by cancer chemotherapy have varying impacts on the daily life of patients, leading to a decline in their quality of life. In the rehabilitation of patients with CRC chemotherapy, we should strengthen evaluation of their degree of fatigue, carry out health education in advance, and use CBT combined with Baduanjin as auxiliary rehabilitation therapy, which can prevent and slow down the decline of cognitive function, and ultimately improve quality of life.

CONCLUSION

Patients with CRC generally have obvious CRF (mainly body fatigue), cognitive impairment, and serious decline in quality of life, which affects their prognosis. CBT combined with Baduanjin exercise can improve fatigue and cognitive impairment of CRC patients undergoing chemotherapy, and improve their quality of life. The quality of life of CRC patients is closely related to their CRF and cognitive level. CBT combined with exercise intervention is worth promoting in the postoperative rehabilitation of cancer patients.

ARTICLE HIGHLIGHTS

Research background

Patients with colorectal cancer (CRC) after chemotherapy are often accompanied with cancer-related fatigue (CRF) and cancer-related cognitive dysfunction, which seriously affects the quality of life and recovery during chemotherapy, but there is no effective treatment.

Research motivation

This study sought to find an effective treatment for cognitive impairment and cancer-related fatigue after chemotherapy for CRC, and to provide a theoretical basis and practical reference for rehabilitation of CRC patients.

Research objectives

This study aimed to explore the effects cognitive behavior therapy (CBT) combined with Baduanjin exercise on CRF, cognitive impairment, and quality of life in patients

with CRC after chemotherapy.

Research methods

Patients with CRC were treated with CBT combined with Baduanjin (experimental group, $n = 27$) or usual care (control group, $n = 28$), and then the changes of cancer-related fatigue, cognitive function, quality of life, and P300 amplitude and latency were compared at baseline, 3 mo, and 6 mo.

Research results

Compared with the baseline values, the cancer-related fatigue, cognitive function, quality of life, and P300 amplitude and latency were significantly better in the experimental group at 3 mo ($P < 0.01$). The cancer-related fatigue, cognitive function, quality of life, and P300 amplitude and latency were significantly better in the experimental group than in the control group (experimental group *vs* control group at 3/6 mo; $P < 0.05$ or $P < 0.01$). The quality of life was negatively correlated with cancer-related fatigue and positively correlated with cognitive function.

Research conclusions

CBT combined with Baduanjin exercise can improve fatigue and cognitive impairment of CRC patients undergoing chemotherapy, and improve their quality of life. The quality of life of CRC patients is closely related to their CRF and cognitive level. CBT combined with exercise intervention is worth promoting in the postoperative rehabilitation of cancer patients.

Research perspectives

This study contributes to the rehabilitation of cognitive impairment and cancer-related fatigue in patients with colorectal cancer after chemotherapy. To confirm and validate the results of this study, a larger scale prospective study would be helpful.

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