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Factors influencing clinical decision-making and health-related quality of life changes in colorectal cancer patients receiving targeted therapy: a multicenter study in China

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Abstract

Objectives The aim of this paper is to assess the current clinical application of targeted therapy in colorectal cancer (CRC), identify factors influencing patients' acceptance of targeted therapy, and evaluate its impact of targeted therapy on patients' health-related quality of life (HRQoL).

Methods This study was based on a national multi-center survey. From March 2020 to March 2021, involved 19 tertiary hospitals across seven regions in China through multi-stage stratified sampling. CRC patients who underwent genetic testing participated. Data on demographic and clinical characteristics, disease knowledge, medical service utilization, medical expenditure, and HRQoL before and after treatment were collected through face-to-face interviews. Logistic regression identified factors affecting therapy acceptance, while the HRQoL changes in pre-and post-treatment were compared by the Mann-Whitney U test.

Results Among 1,468 eligible patients, 79.7% were aged 50+, 60% male, and 31.5% retired. Secondary education was the most common level (30.3%). A total of 62.7% of patients received targeted therapy. Multivariable analysis showed that metastasis at diagnosis, out-of-pocket expenses, and reimbursement ratio were positively associated with targeted therapy ($P < 0.05$), while initial diagnosis stage, region, and genetic testing reimbursement were negatively associated ($P < 0.05$). Post-therapy, patients' quality of life declined significantly ($P < 0.001$), especially in fatigue and financial burden.

Conclusions Our study revealed multiple factors influencing CRC patients' acceptance of targeted therapy and found that targeted therapy may adversely affect HRQoL. These findings emphasize the necessity of implementing more comprehensive patient management strategies to optimize the clinical application of targeted therapy and improve patients' quality of life.

Keywords Colorectal cancer, Targeted treatment, Health-related quality of life, Risk factors

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Introduction

Colorectal cancer (CRC) is the third most prevalent cancer globally and the second leading cause of cancer-related mortality, accounting for approximately 10.2% of all malignant tumor morbidity and 9.3% of mortality [1]. In China, CRC has emerged as a significant public health concern due to its rising incidence. In 2022, around 517,000 new cases and nearly 240,000 deaths were reported [2]. A key concern is that the early symptoms of CRC are often subtle and difficult for patients to detect, leading to a high rate of advanced-stage diagnoses. This issue is particularly pronounced in China, where over 50% of cases are identified at a late stage [3, 4]. Advanced CRC often leads to distant metastasis, and only 10–20% of metastatic lesions can be completely resected through surgery at initial diagnosis [5, 6]. Although traditional treatment methods have made some progress in improving patient prognosis, their effectiveness remains limited, particularly in advanced stages.

Given these challenges in CRC treatment, molecularly targeted therapy provides a new strategy for enhancing treatment effectiveness as a vital part of precision medicine [7, 8]. These targeted therapies play a crucial role in both first-line and second-line treatments for advanced CRC, offering new possibilities for improving patient prognosis. However, clinical evidence indicates that not all patients with identified genetic targets receive targeted therapy. This heterogeneity may be caused by various factors, including but not limited to economic burden, patient awareness, accessibility of medical resources, and clinical decision-making considerations. Despite this, no nationally representative data on CRC patients in China currently exist. Additionally, while targeted therapy has demonstrated significant effects in prolonging survival [9, 10], its overall impact on patients' quality of life remains unclear.

Therefore, this study aims to evaluate the current clinical application of targeted therapies in CRC, identify the factors influencing their adoption, and assess the dynamic changes in patients' quality of life before and after targeted therapy. These findings are expected to aid clinicians in formulating more precise, individualized treatment plans and offering patients well-rounded, evidence-based information for making treatment decisions.

Methods

Study design

This study is a national multicenter cross-sectional investigation, and the study design was discussed in the previous literature [11]. In brief, from March 2020 to March 2021, this study employed a multistage stratified sampling method to conduct a cross-sectional survey in 19 hospitals across 14 cities within seven major regions of China. First, the regions (Eastern, Northern, Southern, Central, Northeast, Southwest, and Northwest) were categorized by geographical location, with two representative cities selected from each region through simple random sampling. Secondly, from each city, at least one tertiary specialized oncology hospital and/or a general hospital was included through convenience sampling. The inclusion criteria for hospitals are: (1) the capacity to offer comprehensive CRC diagnosis and treatment services, encompassing diagnosis, surgery, radiotherapy, chemotherapy, and standard follow-up care; (2) the hospital's patient population should be geographically diverse, capturing the region's disease epidemiology and treatment practices. This design aims to ensure that the study subjects are regionally representative and that clinical practices are generalizable. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). It was submitted to and approved by the independent review board of Henan Cancer Hospital (No. 2019273). The other 18 hospitals were informed and agreed to participate in the study. Informed consent was obtained from all participants.

Study population

Patients were enrolled based on the following criteria: (1) diagnosis of colorectal cancer; (2) aged ≥ 18 years old; (3) underwent genetic testing at any stage; (4) voluntary participation and signed informed consent. Patients with severe physical, cognitive and/or language impairment were excluded.

Data collection

In this study, data on CRC patients' demographics, information on diagnosis, CRC prevention knowledge, and screening, as well as medical expenses were collected through standardized self-report questionnaires, semi-structured interviews (SSQ), and medical records. Furthermore, The Functional Assessment of Cancer Therapy-Colorectal (FACT-C) and the European Organisation for Research and Treatment of Cancer (EORTC QLQ-C30) are reliable and widely used for assessing the quality of life in cancer patients [12, 13]. By selecting 45 items from the two scales, a new scale called FACT-C plus QLQ-C9 was created for this survey, mainly consisting of six functional subscales (physical, social/family, emotional, functional, CRC cancer and cognitive), two symptom subscales (fatigue and sleep disturbance) and a single item regarding financial difficulties. Each item and the overall scores, which include reverse coding where necessary, are calculated and normalized to a scale of 0 to 100, and higher scores indicate better health-related quality of life (HRQoL). The quality of life of patients was collected at two-time points: the first or second day of hospitalization before treatment, and the day after treatment but before discharge. Treatment refers

to interventions like surgery or chemotherapy. Further details about the SSQ and the FACT-C plus QLQ-C9 can be found in a previously published study [11].

The questionnaire underwent pre-survey testing to ensure reliability and validity. All eligible advanced CRC patients were verbally invited to participate in this study by trained investigators. If the patient was unable to answer the questions, their family members were invited to participate in the interview. The survey questionnaire was completed by the patients themselves or filled out by the interviewers during the face-to-face interviews.

Statistical analysis

Continuous variables with normal distribution were presented as mean and standard deviation, while continuous variables with abnormal distribution were presented as median and interquartile range (IQR). Categorical variables were described using frequencies and percentages (%). Univariate and multivariate logistic regression analyses were conducted to identify factors associated with patients' decision to undergo targeted therapy. Variables with $P<0.05$ were considered as candidates for the multivariate regression analysis. Furthermore, the Mann-Whitney U test was employed to compare the differences in quality of life before and after treatment among patients who participated in targeted therapy.

The data were double-entered using Epidata 3.1 software, and statistical analysis were performed using R software (version 4.2.0, R Foundation for Statistical Computing). A two-sided $P<0.05$ was considered statistically significant.

Results

A total of 2,128 CRC patients who had undergone genetic testing were included in the study, of which 1,468 patients were identified with gene mutations suitable for targeted therapy. Among these 1,468 study subjects, 79.7% were over 50 years old, 60% were male, 31.5% had already retired, and 30.3%had an education level of middle school. A total of 921 patients had received targeted therapy, while 547 patients did not undergo targeted therapy during the diagnosis and treatment process.

Table 1 presents the differences in sociodemographic characteristics, clinical features, and health awareness between the targeted therapy and non-targeted therapy groups. Among them, the targeted therapy group was more inclined to be doctor-led, while the non-targeted therapy group tended to be family-led ($P=0.019$). There were also significant differences in the distribution of the two groups across the seven major regions in China ($P<0.001$), with the targeted therapy group more concentrated in the Eastern, Central, and Northeast regions. The targeted therapy group showed a higher incidence of colon cancer. Furthermore, patients receiving targeted therapy showed a higher prevalence of widespread metastasis and a higher proportion of late-stage patients ($P<0.005$). No statistically significant differences were observed between the two groups in other variables and preventive awareness related factors, such as the number of hospitals visited, early screening knowledge, awareness of high-risk factors, and colonoscopy screening.

Table 2 compared the economic status, healthcare expenditure, and medical insurance coverage of the two groups. Compared to the non-targeted therapy group, the targeted therapy group had higher out-of-pocket medical expenditure, greater annual income of children, and higher treatment cost from the perspective of patients ($P<0.05$). Additionally, those without reimbursement for genetic testing, with private insurance, and with a higher reimbursement ratio were more likely to receive targeted therapy ($P<0.05$). There were no significant differences between the two groups in primary bearers of treatment costs and family income. All variables with significant differences ($P<0.05$) from the univariate analysis were included in the multivariate analysis. As shown in Table 3, the results demonstrated that stage at initial diagnosis was significantly associated with targeted therapy (OR = 0.54, $P=0.003$). Compared to patients with no metastasis, those with metastasis were more inclined to choose targeted therapy (ORs ranged from 3.90 to 10.59, $P<0.05$). Compared to the eastern region, patients in the northern, southern, and western regions were less likely to choose targeted therapy (ORs ranged from 0.28 to 0.50, $P<0.05$). Additionally, out-of-pocket medical expenditure was positively associated with the use of targeted therapy (ORs ranged from 2.28 to 14.13, $P<0.05$). The policy of reimbursing only in the patient's registered residence significantly hindered the choice of targeted therapy (OR = 0.19, $P=0.005$). Meanwhile, the higher the reimbursement ratio, the more likely patients were to choose targeted therapy (OR = 1.02, $P<0.001$). Table 4 highlighted the impact of targeted therapy on HRQoL, showing a significant decline from 77.02 to 71.95 after targeted therapy ($P<0.001$), with multiple subscales reflecting this trend. Furthermore, except for social/family well-being, all other subscales showed a significant downward trend ($P<0.05$). The most pronounced declines were observed in the fatigue and financial impacts domains.

Discussion

This study utilized data from a Chinese multicenter survey to investigate the factors affecting the use of targeted therapies in Chinese patients with advanced CRC, as well as the impact of these therapies on patients' HRQoL. The research found that among 1,468 patients with genetic test results suitable for targeted therapy, 62.7% received targeted therapy. This proportion reflects the importance

Table 1 Sociodemographic characteristics, clinical features, and health awareness among colorectal cancer patients with and without targeted therapy

Variables	Overall (*N*, %)	Genetics support targeted therapy		*P*
		Targeted therapy (*N*, %)	Non-targeted therapy (*N*, %)	
	1468 (100)	921 (62.7)	547 (37.3)	
Age				0.16
< 50	298 (20.3)	176 (19.1)	122 (22.3)	
≥ 50	1170 (79.7)	745 (80.9)	425 (77.7)	
Gender				0.334
Male	881 (60.0)	562 (61.0)	319 (58.3)	
Female	587 (40.0)	359 (39.0)	228 (41.7)	
Marital Status				
Married	1389 (94.6)	870 (94.5)	519 (94.9)	0.823
Other	79 (5.4)	51 (5.5)	28 (5.1)	
Education				0.053
Primary school or below	332 (22.6)	197 (21.4)	135 (24.7)	
Middle school	445 (30.3)	265 (28.8)	180 (32.9)	
High school	363 (24.7)	243 (26.4)	120 (21.9)	
College and above	328 (22.3)	216 (23.5)	112 (20.5)	
Occupation				0.448
Professional and Public Service Sector	168 (11.4)	112 (12.2)	56 (10.2)	
Freelancers/Self-employed	153 (10.4)	91 (9.9)	62 (11.3)	
Labor and Services Sector	402 (27.4)	251 (27.3)	151 (27.6)	
Retired	463 (31.5)	299 (32.5)	164 (30.0)	
Unknown	282 (19.2)	168 (18.2)	114 (20.8)	
Family Member in Medical Profession				0.633
Yes	208 (14.2)	127 (13.8)	81 (14.8)	
No	1259 (85.8)	794 (86.2)	465 (85.2)	
Patient Autonomy in Decision-Making				0.019
Patient-dominated	829 (56.6)	517 (56.3)	312 (57.1)	
Family-dominated	217 (14.8)	121 (13.2)	96 (17.6)	
Doctor-dominated	419 (28.6)	281 (30.6)	138 (25.3)	
Location of Cancer				0.001
Colon cancer	744 (50.7)	485 (52.7)	259 (47.3)	
Rectal cancer	693 (47.2)	426 (46.3)	267 (48.8)	
Other	31 (2.1)	10 (1.1)	21 (3.8)	
Reason for Initial Consultation				0.056
Symptomatic self-presentation	1252 (85.8)	768 (84.1)	484 (88.6)	
Physical examination findings	102 (7.0)	72 (7.9)	30 (5.5)	
Detection of CRC during screening or treatment of other diseases	105 (7.2)	73 (8.0)	32 (5.9)	
Stage at Initial Diagnosis				< 0.001
Advance Stage	1288 (87.7)	855 (92.8)	433 (79.2)	
Early Stage	180 (12.3)	66 (7.2)	114 (20.8)	
Metastasis at initial diagnosis				< 0.001
No metastasis	678 (46.5)	311 (33.8)	367 (68.1)	
Metastasis only in the liver	322 (22.1)	258 (28.0)	64 (11.9)	
Metastasis only in the lungs	68 (4.7)	53 (5.8)	15 (2.8)	
Metastasis in both the liver and lungs	100 (6.9)	88 (9.6)	12 (2.2)	
Metastasis in other or multiple areas	291 (19.9)	210 (22.8)	81 (15.0)	
Hospital Type				0.214
Cancer specialty hospital	893 (60.8)	572 (62.1)	321 (58.7)	
General hospital	575 (39.2)	349 (37.9)	226 (41.3)	
Region				< 0.001
Eastern	287 (19.6)	208 (22.6)	79 (14.4)	

Table 1 (continued)

Variables	Overall (*N*, %)	Genetics support targeted therapy		*P*
		Targeted therapy (*N*, %)	Non-targeted therapy (*N*, %)	
Northern	333 (22.7)	186 (20.2)	147 (26.9)	
Southern	205 (14.0)	105 (11.4)	100 (18.3)	
Central	247 (16.8)	160 (17.4)	87 (15.9)	
Northeast	78 (5.3)	66 (7.2)	12 (2.2)	
Southwest	241 (16.4)	148 (16.1)	93 (17.0)	
Northwest	77 (5.2)	48 (5.2)	29 (5.3)	
Number of Hospitals Visited				0.099
1	1189 (81.9)	759 (83.2)	430 (79.6)	
≥ 2	263 (18.1)	153 (16.8)	110 (20.4)	
Knowledge of Early Screening				0.771
Yes	251 (17.1)	160 (17.4)	91 (16.6)	
No	1217 (82.9)	761 (82.6)	456 (83.4)	
Awareness of High-Risk Factors				0.485
Yes	536 (36.5)	343 (37.2)	193 (35.3)	
No	932 (63.5)	578 (62.8)	354 (64.7)	
Knowledge of Treatment Options				0.713
Yes	631 (43.0)	392 (42.6)	239 (43.7)	
No	837 (57.0)	529 (57.4)	308 (56.3)	
Colonoscopy Screening				0.814
Yes	49 (3.3)	32 (3.5)	17 (3.1)	
No	1417 (96.7)	887 (96.5)	530 (96.9)	

of targeted therapy in the treatment regimen for late-stage CRC, but also emphasizes that a substantial number of patients did not adopt this potentially beneficial treatment. Multivariate logistic regression analysis identified several key factors influencing targeted therapy adoption, including initial diagnosis stage, metastasis presence, geographic region, out-of-pocket medical expenses, genetic testing reimbursement, and reimbursement proportion. Additionally, the study found that targeted therapy had the negative impact on the quality of life of these patients.

The findings of this study indicate that patients who had metastatic disease at diagnosis, especially those with liver and lung metastases, were more likely to receive targeted therapy. This trend suggests that clinicians consider more aggressive treatment options in cases with higher progression risks and poorer prognosis. Such a tendency could result from recent advances in understanding the mechanisms of CRC metastasis, providing new scientific rationale and potential therapeutic targets for targeted treatment [14]. Previous study demonstrated that tumor-secreted FGF19 promotes liver metastasis in CRC by inducing inflammatory cancer-associated fibroblasts (iCAF), which further stimulate the formation of neutrophil extracellular traps (NETs), highlighting a novel therapeutic target for liver metastasis [5]. Moreover, professional guidelines from NCCN and ESMO also underscore the importance of targeted therapy in managing advanced metastatic CRC [15, 16]. In contrast, early-stage patients were less likely to receive targeted therapy, possibly due to a focus on surgical and minimally invasive options [17, 18].

Economic factors also play a critical role in decision-making regarding targeted therapy for patients with advanced CRC. The results indicate that patients with higher out-of-pocket medical expenses are more likely to receive targeted therapies. This seemingly paradoxical finding highlights a complex reality: Patients with better economic conditions have a stronger ability to pay, allowing them to afford the high costs of targeted therapy, while low-income patients may be forced to forgo such treatments due to financial pressure. This underscores the issue of healthcare inequality and illustrates the strong link between access to innovative therapies and patients' financial status. Consistent with previous research, a cross-sectional study including 1208 cancer patients found similar results regarding financial toxicity among cancer patients in China, identifying lower household income as a significant predictor of financial toxicity [19]. Similarly, a cross-sectional study analysing the financial toxicity of patients with advanced CRC in China also found that household monthly income is one of the key factors influencing subsequent treatment decisions [20].

Furthermore, reimbursement policies for genetic testing had a significant impact on the probability of patients receiving targeted therapy. When reimbursement was limited to the patient's residence, the probability of

Table 2 Economic status, healthcare expenditure, and medical insurance coverage among colorectal cancer patients with and without targeted therapy

Variables	Overall (*N*, %)	Genetics support targeted therapy		*P*
		Targeted therapy (*N*, %)	Non-targeted therapy (*N*, %)	
	1468 (100)	921 (62.7)	547 (37.3)	
Primary Bearers of Treatment Costs				0.112
Self/Spouse	674 (45.9)	409 (44.4)	265 (48.4)	
Children	171 (11.6)	101 (11.0)	70 (12.8)	
Parents/Children	425 (29.0)	286 (31.1)	139 (25.4)	
Others	198 (13.5)	125 (13.6)	73 (13.3)	
Out-of-pocket medical expenditure(10,000 CNY)				< 0.001
< 5	227 (15.5)	94 (10.2)	133 (24.3)	
5–10	572 (39.0)	304 (33.0)	268 (49.0)	
10–20	400 (27.3)	292 (31.7)	108 (19.7)	
> 20	268 (18.3)	230 (25.0)	38 (6.9)	
Family income (10,000 CNY)				0.178
No Income	207 (14.1)	122 (13.3)	85 (15.6)	
< 5	570 (39.0)	345 (37.6)	225 (41.3)	
5–10	417 (28.5)	273 (29.7)	144 (26.4)	
10–20	202 (13.8)	130 (14.2)	72 (13.2)	
> 20	67 (4.6)	48 (5.2)	19 (3.5)	
Annual Income of Children(10,000 CNY)				0.001
No Income	284 (19.5)	173 (19.0)	111 (20.4)	
< 5	368 (25.3)	221 (24.3)	147 (27.0)	
5–10	460 (31.7)	268 (29.5)	192 (35.3)	
10–20	232 (16.0)	169 (18.6)	63 (11.6)	
> 20	109 (7.5)	78 (8.6)	31 (5.7)	
Cost of colorectal cancer treatment from the perspective of patients(10,000 CNY)				< 0.001
< 5	355 (24.3)	192 (21.0)	163 (29.9)	
5–10	460 (31.5)	269 (29.4)	191 (35.0)	
10–20	368 (25.2)	243 (26.6)	125 (22.9)	
> 20	278 (19.0)	211 (23.1)	67 (12.3)	
Reimbursement for Genetic Testing				0.031
Reimbursable	644 (44.0)	381 (41.5)	263 (48.1)	
Not reimbursable	801 (54.7)	526 (57.3)	275 (50.3)	
Reimbursable only in patient's registered area	20 (1.4)	11 (1.2)	9 (1.6)	
Health Insurance Type				0.003
Public	1281 (87.3)	785 (85.2)	496 (90.7)	
Private	180 (12.3)	133 (14.4)	47 (8.6)	
None	7 (0.5)	3 (0.3)	4 (0.7)	
Reimbursement Ratio	60.00 50.00, 70.00	60.00 50.00, 70.00	60.00 50.00, 70.00	< 0.001

receiving targeted therapy decreased (OR: 0.19), indicating the importance of improving insurance policies to facilitate access to precision medicine. Previous studies have similarly shown that expansion of insurance coverage is closely associated with increased use of innovative cancer therapies [21–23].

It is noteworthy that the research revealed regional differences in patients' decisions regarding targeted therapy. Compared to the eastern region, patients in the northern, southern, southwestern, and northwestern regions have a significantly lower likelihood of receiving targeted therapy. These disparities not only reflect the uneven distribution of economic development and medical resources but may also be related to systemic gaps in healthcare infrastructure. The eastern region has a clear advantage in the allocation of medical resources, with a concentration of specialized cancer centers and experienced clinicians, enabling the delivery of precise genetic testing and targeted treatment plans [24, 25]. In contrast, underdeveloped areas face resource shortages, resulting in limited diagnostic and treatment capabilities [26]. This finding aligns with Yang et al.'s (2017) research, which

Table 3 Multivariate analysis of patients receiving targeted therapy

	β-coefficient	OR (95% CI)	*P*
Patient Autonomy in Decision-Making			
Patient-dominated	Reference	1	
Family-dominated	-0.34	0.71(0.48–1.05)	0.084
Doctor-dominated	0.21	1.23(0.90–1.69)	0.191
Location of Cancer			
Colon cancer	Reference	1	
Rectal cancer	-0.039	0.96(0.74–1.26)	0.775
Other	-1	0.37(0.13–1.01)	0.056
Stage at Initial Diagnosis			
Advance Stage	Reference	1	
Early Stage	-0.609	0.54(0.36–0.81)	0.003
Metastasis at initial diagnosis			
No metastasis	Reference	1	
Metastasis only in the liver	1.777	5.91(4.06–8.72)	< 0.001
Metastasis only in the lungs	1.598	4.94(2.56–10.09)	< 0.001
Metastasis in both the liver and lungs	2.36	10.59(5.45–22.20)	< 0.001
Metastasis in other or multiple areas	1.36	3.90(2.68–5.72)	< 0.001
Region			
Eastern	Reference	1	
Northern	-0.691	0.50(0.32–0.78)	0.002
Southern	-1.032	0.36(0.21–0.60)	< 0.001
Central	-0.366	0.69(0.42–1.15)	0.159
Northeast	0.722	2.06(0.96–4.66)	0.071
Southwest	-0.963	0.38(0.23–0.62)	< 0.001
Northwest	-1.273	0.28(0.15–0.54)	< 0.001
Number of Hospitals Visited			
1	Reference	1	
> 1	0.013	1.01(0.72–1.43)	0.941
Out-of-pocket medical expenditure(10,000 CNY)			
< 5	Reference		
5–10	0.825	2.28(1.57–3.33)	< 0.001
10–20	1.838	6.29(4.12–9.68)	< 0.001
> 20	2.648	14.13(8.47–24.08)	< 0.001
Annual Income of Children(10,000 CNY)			
No Income	Reference	1	
< 5	0.165	1.18(0.78–1.77)	0.429
5–10	-0.08	0.92(0.63–1.35)	0.68
10–20	0.471	1.60(1.00-2.58)	0.051
> 20	0.277	1.32(0.72–2.44)	0.372
Cost of colorectal cancer treatment from the perspective of patients(10,000 CNY)			
< 5	Reference	1	
5–10	0.171	1.19(0.83–1.70)	0.348
10–20	0.146	1.16(0.76–1.76)	0.492
> 20	0.419	1.52(0.93–2.50)	0.097
Reimbursement for Genetic Testing			
Reimbursable	Reference	1	
Not reimbursable	-0.192	0.83(0.60–1.13)	0.23
Reimbursable only in patient's registered area	-1.655	0.19(0.06–0.61)	0.005
Health Insurance Type			
Public	Reference	1	
Private	0.191	1.21(0.78–1.91)	0.406
None	0.233	1.26(0.15–9.88)	0.826
Reimbursement Ratio	0.018	1.02(1.01–1.03)	< 0.001

Table 4 Comparison of Health-Related quality of life (HRQoL) scores before and after targeted therapy among patients with colorectal cancer

	Number of items	Before targeted therapy (*N* = 921)	After targeted therapy (*N* = 921)	*P*
Overall HRQoL	45	77.02 (0.45)	71.95 (0.42)	< 0.001
FACT-C				
Physical well-being	10	86.70 (0.46)	75.74 (0.47)	< 0.001
Social/Family well-being	7	82.40 (0.72)	83.22 (0.70)	0.442
Emotional well-being	5	77.31 (0.84)	74.12 (0.70)	< 0.001
Functional well-being	7	63.23 (0.80)	51.88 (0.76)	< 0.001
Colorectal cancer subscale	7	66.76 (0.58)	62.61 (0.54)	< 0.001
EORTCQLQ-C30				
Functional scales and/or items				
Physical	1	93.57 (0.67)	89.66 (0.73)	< 0.001
Cognitive	1	85.34 (0.72)	76.87 (0.87)	< 0.001
Emotional	2	79.42 (0.85)	77.35 (0.75)	< 0.001
Social	2	75.67 (0.96)	63.22 (0.91)	< 0.001
Symptom items				
Fatigue	1	88.84 (0.70)	75.71 (0.87)	< 0.001
Sleep disturbance	1	73.40 (0.99)	70.41 (0.97)	0.006
Financial impacts	1	74.24 (1.03)	56.32 (1.05)	< 0.001

noted that cancer mortality rates are significantly higher in regions with low per capita GDP compared to those with high GDP, partly due to insufficient allocation of medical resources [27]. Similarly, the American Cancer Society's 2023 report on cancer disparities in the United States highlighted that mortality rates for CRC were 23% higher for men and 21% higher for women in economically disadvantaged regions compared to affluent areas [28].

The comparative analysis of HRQoL before and after targeted therapy indicated a significant decline in patients' overall HRQoL post-treatment. This result suggests that while targeted therapy may be effective in tumor control, it can adversely affect patients' quality of life. The decline may be due to the side effects and physiological changes caused by the treatment, as well as the psychological adaptation to the disease and its treatment [29]. Previous studies have shown mixed results regarding the impact of targeted therapies on quality of life. Hu et al. evaluated HRQoL in patients receiving adjuvant therapy with aumolertinib in real-world settings and found gradual improvements in overall health status/quality of life and functional scales, although symptom scale scores gradually decreased [30]. Similarly, a clinical trial of 351 breast cancer patients showed that treatment with trastuzumab improved patients' quality of life [31]. These differences may reflect differences between targeted drugs, as well as factors such as patient characteristics, treatment stage and length of follow-up. These differences may be attributed to variations in targeted drugs, patient characteristics, treatment stages, and length of follow-up.

The current study had several limitations. First, despite employing a multicenter sampling strategy, this study was primarily conducted in large urban medical centers, potentially introducing selection bias and affecting the external validity of the findings, particularly concerning patients from rural and underdeveloped regions. Second, the HRQoL survey relied mainly on self-reported data, which may be prone to recall bias and subjectivity. Third, in actual clinical practice, patients may receive combinations or sequential treatments with multiple targeted therapies. However, the study's questionnaire design did not account for this complexity, making it difficult to distinguish the specific effects of various targeted therapies on quality of life, and potentially masking the unique effects of certain treatments. Fourth, the questionnaire in this study did not specifically differentiate the effects of different targeted therapies. Future research could incorporate data related to targeted drugs to systematically explore the relationship between the efficacy of targeted therapies and the subtypes of gene mutations. Finally, this study solely evaluated the immediate alterations in HRQoL following targeted therapy, without monitoring long - term outcomes. Certain targeted therapies may exhibit delayed adverse effects or confer potential long - term survival advantages, requiring further investigation through longitudinal studies. Future research endeavors should integrate HRQoL assessments at multiple temporal intervals to better capture the dynamic impact of targeted therapy on patients' quality of life.

In conclusion, this study provides a comprehensive analysis of the factors influencing the decision-making process for targeted therapy in CRC patients. Additionally, it reveals that targeted therapy may adversely affect

patients' quality of life. These findings offer valuable evidence for the clinical decision-making of CRC patients, enabling a more holistic consideration of key factors when evaluating treatment options, thereby making more reasonable choices to achieve the best therapeutic effect.

Abbreviations

CRC	Colorectal cancer
HRQoL	Health-related quality of life
FACT-C	The functional assessment of cancer therapy-colorectal
IQR	Interquartile range
iCAF	Inducing inflammatory cancer-associated fibroblasts
NETs	Neutrophil extracellular traps
ASMR	Age-standardised mortality rates

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Author contributions
ZYL, CXF, and HWL contributed to the conception and design. ZYL drafted the manuscript. CXF contributed to data curation and data analysis. SKZ and YLQ administratively supported this study. YL, HFX, YQZ, XZ and YQY made substantial contribution to the study protocol. All authors contributed to the article and approved the submitted version.

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Data availability
The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). It was submitted to and approved by the independent review board of Henan Cancer Hospital (No. 2019273). Informed consent was obtained from all participants.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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