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Comparative characteristics of early-onset vs. late-onset advanced colorectal cancer: a nationwide study in China

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Abstract

Background The incidence of early-onset colorectal cancer (EOCRC, diagnosed in patients under the age of 50 years) has been increasing around the world. Here, we aimed to systematically identify distinctive features of EOCRC.

Methods From 2020 to 2021, we conducted a nationwide survey in 19 hospitals, collecting data on advanced CRC patients' demographics, clinical features, disease knowledge, medical experiences, expenditures, and health-related quality of life (HRQOL). We compared these features between EOCRC and late-onset colorectal cancer (LOCRC, \geq 50 years old) groups and analyzed the association between EOCRC and HRQOL using multivariate linear regression.

Findings In total, 991 patients with EOCRC and 3581 patients with LOCRC were included. Compared to the LOCRC group, the EOCRC group had higher levels of education, were more informed about the risk factors for CRC, were more likely to have widespread metastases throughout the body, were more inclined to undergo gene testing, and were more likely to opt for targeted therapy, radiotherapy, and chemotherapy. However, HRQOL in the EOCRC group was similar to that of the LOCRC group, and no significant association was observed between EOCRC and HRQOL (beta: -0.753, *P* value: 0.307).

Interpretation In Chinese patients, EOCRC patients had more aggressive features. Despite undergoing more intensified treatments and gene testing, they had similar HRQOL compared with LOCRC. These findings advocate for a more tailored approach to treatment, especially for young CRC patients with advanced TNM stages and metastasis.

Keywords Early-onset colorectal cancer, Late-onset colorectal cancer, Clinical epidemiology features, Health-related quality of life

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Introduction

Colorectal cancer (CRC) is the third most common cancer worldwide and the second leading cause of cancerrelated mortality [1]. Based on the age at diagnosis, CRC can be classified as the early-onset colorectal cancer (EOCRC), which is diagnosed before 50 years of age, and the late-onset colorectal cancer (LOCRC), which is diagnosed at or after 50 years of age [2]. The LOCRC incidence has generally decreased since the early 1990s [1], especially in western countries, which is likely attributable to population-based screening with colonoscopy. In contrast, the incidence of EOCRC has steadily increased by 2% annually [3–5]. The reasons for this increase in EOCRC, including potential unique biological characteristics compared to LOCRC, remain unclear.

Multiple studies have demonstrated that EOCRC are more likely to exhibit symptoms, including haematochezia and abdominal pain, to occur in the left colon, have more aggressive histopathology, and have a longer delay from symptom onset to diagnosis [2-6] Regarding the treatment patterns, the EOCRC group has more intensified surgical and perioperative treatment than the LOCRC group [7]. It is reported that the mutations of PIK3CA, BRAF, and KRAS were different between EOCRC and LOCRC patients according to different tumor locations [8-10]. To date, differences between EOCRC and LOCRC have been primarily investigated in developed Western countries. However, nationwide studies among EOCRC patients in China are generally lacking, especially regarding the demographic and clinicopathological features, awareness of CRC, treatment, and health-related quality of life (HRQOL) in EOCRC patients.

To provide a clearer landscape of the characteristics of EOCRC in Chinese patients, we conduct a nationwide survey, comparing the demographic, clinicopathological features, disease knowledge, treatment, and HRQOL, aimed at identity the characteristics of the EOCRC and LOCRC among CRC patients in China.

Methods

Study design

This is a nationwide multicenter cross-sectional survey and the comprehensive study design has been previously published [11]. The study was conducted from March 2020 to March 2021. Advanced colorectal cancer patients were sampled using a multi-stage sampling method. In the first stage, two cities of each geographic regions (Eastern China, Northern China, Central China, Southern China, Northeast China, Southwest China, and Northwest China) of Chinese mainland were selected by simple random sampling. In the second stage, one tertiary cancer hospital and/or one general hospital were selected in each city with inclusion on the basis that (1)

they can provide diagnosis, surgery, radiotherapy, chemotherapy and routine follow- up care for patients with CRC; and (2) visiting patients are from different parts of the region. Finally, a total of 19 hospitals were selected. The detailed information on enrollment data for 19 hospitals from 7 regions is presented in Fig. 1 and Table S1.

In the present study, the primary objective is to compare the demographic, clinical features, disease knowledge, and HRQOL between EOCRC and LOCRC patients. For secondary objectives, we delve into the treatment patterns, factors influencing HRQOL, and the variations in disease management practices between EOCRC and LOCRC patients.

Inclusion and exclusion criteria

Patients who met the following inclusion criteria were included: (1) are diagnosed with stage III or IV CRC at the survey, (2) are aged ≥ 18 years old, (3) are inpatients and (4) provide the informed consent. Patients will be excluded if they had severe physical, cognitive and/or verbal impairments that would interfere with a patient's ability to complete the questionnaire.

Measurements

Demographic and clinicopathologic characteristics

Demographic data were collected through a standardized self-report questionnaire, including age at the first diagnosis of CRC, gender, marital status, education level, geographic region, and occupation. Clinicopathological characteristics included the site of cancer occurrence (colon or rectum), pathological TNM stage at first diagnosis, metastatic status at the survey, the reason for the initial hospital visit, and the number of hospitals visited.

Awareness of CRC risk factors, screening, and treatment

Patients' awareness regarding high-risk factors for colorectal cancer, CRC screening procedures, and treatment options before their diagnosis was gathered through a semi-structured questionnaire (SSQ). The SSQ was developed following the Chinese guidelines [12, 13]. It comprises three multiple-choice questions, and detailed information on the questions is presented in Table S2. Further details about the SSQ can be found in a previously published study [11].

Patients' experiences with CRC screening, diagnosis, and treatment

Another SSQ was employed to gather information concerning CRC screening, diagnosis, and treatment. Patient screening history data were collected, including whether the patient had undergone screening, and information about barriers to not having a colonoscopy was collected based on patient self-reports. These barriers included lack of awareness, insufficient time for a colonoscopy,

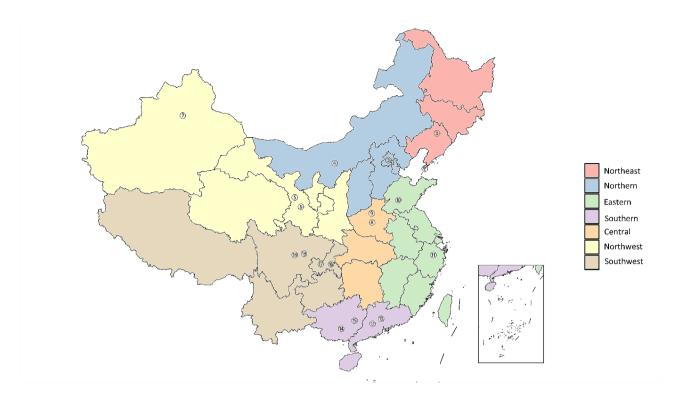


Fig. 1 Map of the 19 hospitals and geographical regions in China. Note The corresponding hospitals for each number are detailed in Table S1

concerns about the discomfort associated with the procedure, cost-related challenges, waiting time for colonoscopy appointments, and issues with insurance coverage. With regards to CRC diagnosis and treatment, the following information was collected based on patients' selfreports: (1) the utilization of gene testing, any barriers encountered, and the results of gene testing. (2) the adoption of currently available treatment modalities, such as targeted therapy, surgery, radiotherapy, chemotherapy, endoscopic treatment, and immunotherapy.

Medical expenditure

Medical expenses data was collected either from the medical records, or through patients' self-reports. The gathered information will encompass patients' out-ofpocket expenditures related to CRC diagnosis and treatment, reimbursement rates for all medical costs, annual household income, the perspective of patients on the cost of colorectal cancer treatment, and the type of health insurance.

Health-related quality of life

Health-related quality of life (HRQOL) was assessed based on two questionnaires: the Chinese Functional Assessment of Cancer Therapy-Colorectal (FACT-C) V.4 and the Chinese version of the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 V.3. The FACT-C V.4 comprises 36 items distributed across five function subscales: physical, social/family, emotional, functional, and a colorectal cancer subscale [11, 14, 15]. Meanwhile, the traditional Chinese version of EORTC QLQ-C30 V.3 includes 30 items grouped into five function subscales (physical, role, emotional, cognitive, and social), nine symptom subscales (fatigue, nausea/vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhoea, and financial difficulties), and a global health/QOL subscale [16, 17]. In this study, a scale named FACT-C-plus-QLQ-C9 was created, consisting of 45 items selected based on expert opinions. This scale includes all FACT-C items along with nine items from QLQ-C30, as outlined in Table S3. The self-developed scale covers six functioning subscales (physical, social/ family, emotional, functional, colorectal cancer subscale, and cognitive), two symptom subscales (fatigue and sleep disturbance), and one item related to financial difficulties. Higher scores on the functioning subscales and lower scores on the symptom subscales indicate a better quality of life. The Chinese versions of FACT-C and EORTC QLQ-C30 have been validated in prior studies [14–17].

Patients' quality of life was assessed after CRC treatment. The summary score of HRQOL for each patient will be calculated across all items, including functioning scales and symptom scales (with inverted scores), resulting in a range from 0 to 180. A higher score indicates a better HRQOL. The Cronbach's α coefficient of HRQOL in our questionnaire was 0.80.

Statistical analysis

Categorical data were described by frequencies and percentages, and continuous data using standard deviations (SD). The *t*-test, chi-square test, and Mann–Whitney U test were used to compare the characteristics of the EOCRC and LOCRC groups. Multivariate regressions were conducted to evaluate the associations between early diagnosis and HRQOL. The following variables were adjusted in multivariate regressions: HRQOL before treatment, sex, cancer location, education level, and TNM stage at initial diagnosis. Statistical significance was set at a *P*-value<0.05. Data analysis was performed using R software (version 4.2.0, R Foundation for Statistical Computing).

Results

A total of 4572 cases of CRC were included in this study. A flowchart of the patient selection process is shown in Fig. S1. Of the included patients, 59.5% were men; 54.5% had rectal cancer; and 37.5% had metastasis. The age distribution at the time of diagnosis is presented in Fig. S2, and the median age at diagnosis was 59.42 years. Patients were classified into two groups based on their age at diagnosis: EOCRC, < 50 years (N=991), and LOCRC, \geq 50 years (N=3581).

Clinicopathologic characteristics of patients with EOCRC and LOCRC are summarized in Table 1. In terms of education level, the EOCRC group had a higher percentage of patients with a university/specialty degree or above (EOCRC=27.9%; LOCRC=12.7%) and a lower percentage of those with primary school education or below (EOCRC=16.2%; LOCRC=32.5%) than that in the LOCRC group. Additionally, the patients with EOCRC exhibited a higher prevalence of widespread metastases (EOCRC=19.7%; LOCRC=14.1%) and a greater frequency of hospital visits (EOCRC=2.10; LOCRC=1.89). However, there were no statistically significant differences among the two groups concerning the location of cancer occurrence, the TNM stage at the time of the first diagnosis, or the reasons for the initial hospital visit.

Table 2 summarizes the characteristics of disease knowledge, medical experience, and expenditure. Compared with the LOCRC group, the EOCRC group had a larger proportion of patients knowing about CRC risk factors and screening, although this difference was not statistically significant. Additionally, more EOCRC patients underwent gene testing (EOCRC=56.7%; LOCRC=44.4%; P<0.001). There were no significant differences in *RAS*, *BRAF* mutations, or microsatellite instability (MSI) among two groups. Regarding the treatment modalities, the EOCRC group exhibited a higher percentage of patients opting for targeted therapy, radiotherapy, and chemotherapy. In terms of medical expenditure, there were significant differences in the out-of-pocket

medical expenditure, medical expenditure reimbursement ratio, annual household income, and health insurance among the two groups.

Table 3 presents the HRQOL scores for patients with EOCRC and LOCRC. Compared with the LOCRC group, the EOCRC group did not exhibit a significant difference in the overall HRQOL score (EOCRC=127.63; LOCRC=128.33; P=0.441). However, concerning the subscales, the EOCRC group had a notably higher score in the physical scale of EORTC QLQ-C30 when compared to the LOCRC group, and it also experienced a more significant financial impact. No significant differences were observed in the scores of other subscales between the EOCRC and LOCRC groups. In patients with CRC, multivariate analysis demonstrates that there is no significant association between early diagnosis of CRC and HRQOL (beta: -0.753, P value: 0.307). The estimated effects of the regression analysis are presented in Table S4.

Discussion

Based on this multicenter, cross-sectional study, we conducted a comprehensive evaluation of the clinical profiles of both EOCRC and LOCRC patients in China. We found that EOCRC patients generally had higher education levels and a higher incidence of widespread metastases. Additionally, they were more prone to undergo gene testing and opt for aggressive treatments like targeted therapy, radiotherapy, and chemotherapy. Despite these differences, their HRQOL was similar to that of LOCRC patients, a finding that merits further investigation into the contributing factors. These unique characteristics of EOCRC underscore the necessity of a thorough evaluation of patient subgroups and indicate a need for tailored screening strategies and treatment protocols, especially in younger demographics.

In this cross-sectional study, we found that EOCRC patients exhibited higher levels of education, greater household income, and a more comprehensive understanding of CRC in comparison to LOCRC patients. This finding may be attributed to the age difference between EOCRC and LOCRC patients. The EOCRC group, comprising younger patients, tended to have received higher levels of education, reflecting the evolving education landscape in China. Patients with higher education levels tended to have higher incomes and more disease knowledge.

Our results revealed that the EOCRC group tends to exhibit more widespread metastases and a more advanced TNM stage than the LOCRC group, though this difference in the TNM stage did not reach statistical significance. Our findings were consistent with previous studies in the Western population and Chinese, which showed that the EOCRC group had a higher risk

Table 1 Clinicopathologic characteristics of patients with early-onset and late-onset colorectal cancer

	Overall (N=4572)	EOCRC, < 50 years (N=991)	LOCRC, ≥ 50 years (N=3581)	P value
Age at diagnosis, years	58.64 (11.71)	42.24 (6.85)	63.18 (8.20)	< 0.001
Sex				0.001
Male	2720 (59.5)	544 (54.9)	2176 (60.8)	
Female	1852 (40.5)	447 (45.1)	1405 (39.2)	
Marital status				0.001
Married	4318 (94.1)	911 (91.9)	3390 (94.7)	
Not married/divorced/widowed	270 (5.9)	80 (8.1)	190 (5.3)	
Education level				< 0.001
Primary school or below	1325 (29.0)	161 (16.2)	1164 (32.5)	
Middle school	1475 (32.3)	343 (34.6)	1132 (31.6)	
High school/specialized secondary schools	1037 (22.7)	211 (21.3)	826 (23.1)	
University/specialty or above	732 (16.0)	276 (27.9)	456 (12.7)	
Region				< 0.001
Eastern	1312 (28.7)	233 (23.5)	1079 (30.1)	
Northern	563 (12.3)	112 (11.3)	451 (12.6)	
Southern	665 (14.5)	197 (19.9)	468 (13.1)	
Central	689 (15.1)	141 (14.2)	548 (15.3)	
Northeast	364 (8.0)	60 (6.1)	304 (8.5)	
Southwest	652 (14.3)	165 (16.6)	487 (13.6)	
Northwest	327 (7.2)	83 (8.4)	244 (6.8)	
Occupation				< 0.001
Government and public sector personnel	653 (14.3)	271 (27.3)	382 (10.7)	
Service workers, migrant workers, and individuals	1726 (37.8)	472 (47.6)	1254 (35.0)	
Unemployment, layoffs, etc.	1929 (42.2)	181 (18.3)	1748 (48.8)	
Unknow	264 (5.8)	67 (6.8)	197 (5.5)	
Location of cancer				0.107
Colon	2054 (45.5)	83 (53.5)	1587 (44.8)	
Rectum	2463 (54.5)	72 (46.5)	1953 (55.2)	
Pathological TNM stage at first diagnosis				0.032
	110 (2.5)	19 (2.0)	91 (2.7)	
11	772 (17.6)	141 (14.7)	631 (18.4)	
11	1964 (44.7)	446 (46.6)	1518 (44.2)	
IV	1545 (35.2)	352 (36.7)	1193 (34.8)	
Metastasis at first diagnosis				< 0.001
No metastasis	2842 (62.5)	598 (60.9)	2244 (63.0)	
With liver metastasis only	639 (14.1)	126 (12.8)	513 (14.4)	
With lung metastasis only	179 (3.9)	34 (3.5)	145 (4.1)	
With both liver and lung metastases	191 (4.2)	31 (3.2)	160 (4.5)	
Widespread metastases throughout the body	695 (15.3)	193 (19.7)	502 (14.1)	
Reason for the first hospital visit				0.548
Observation of suspected symptoms by patients themselves	4003 (88.1)	882 (89.2)	3121 (87.7)	
Physical examination findings	265 (5.8)	51 (5.2)	214 (6.0)	
Detection of CRC during screening or treatment of other diseases	278 (6.1)	56 (5.7)	222 (6.2)	
Number of visited hospital	1.94 (0.81)	2.10 (0.83)	1.89 (0.80)	< 0.001

Abbreviations EOCRC, Early-onset colorectal cancer; LOCRC, Late-onset colorectal cancer

Values are presented as mean (standard deviations) for continuous variables or n (%) for categorical variables

of lymph node metastases [18] compared to the LOCRC group. A previous study revealed that the advanced TNM stage at diagnosis in EOCRC patients does not seem to be explained simply by the longer time to diagnosis, suggesting that biological factors may be important determinants

of the TNM stage at diagnosis [19]. Although tumor biology may be an important determinant of the TNM stage at diagnosis, clinicians need to recognize CRC alarm symptoms, family history, and genetic syndromes, to Table 2 Disease knowledge, medical experience, and expenditure in patients with early-onset and late-onset colorectal cancer

	Overall (N=4572)	EOCRC, < 50 years (N = 991)	LOCRC, \geq 50 years (N = 3581)	P value
Awareness of CRC risk factors, yes	1591 (34.9)	366 (37.1)	1225 (34.3)	0.107
Awareness of CRC screening, yes	689 (15.1)	169 (17.1)	520 (14.6)	0.055
Awareness of CRC treatment, yes	2019 (44.2)	441 (44.5)	1578 (44.1)	0.827
Undergoing the colonoscopy before the first diagnosis, yes	120 (2.6)	29 (2.9)	91 (2.5)	0.575
Barriers to undergo colonoscopy				
Lack of awareness, yes	3868 (87.0)	834 (86.8)	3034 (87.1)	0.865
No time for a colonoscopy, yes	368 (8.3)	93 (9.7)	275 (7.9)	0.087
Heard that colonoscopy is a painful procedure, yes	716 (16.1)	141 (14.7)	575 (16.5)	0.189
The cost of colonoscopy is high, yes	172 (3.9)	31 (3.2)	141 (4.0)	0.258
Waiting in line for colonoscopy appointment, yes	172 (3.9)	42 (4.4)	130 (3.7)	0.414
Insurance doesn't cover it, yes	97 (2.2)	22 (2.3)	75 (2.2)	0.803
Undergoing gene testing, including RAS, BRAF, and MSI, yes	1974 (47.1)	518 (56.7)	1456 (44.4)	< 0.001
Barriers to undergo gene testing				0.052
Target therapy is not accepted (other treatment options are considered to be sufficient)	357 (16.1)	45 (11.3)	312 (17.2)	
The test is too expensive and not reimbursable	528 (23.8)	107 (26.8)	421 (23.2)	
Anxious to receive treatment and unwilling to wait for genetic test results	125 (5.6)	18 (4.5)	107 (5.9)	
Plan to blind-eat targeted drugs	32 (1.4)	6 (1.5)	26 (1.4)	
Lack of knowledge	952 (43.0)	183 (45.9)	769 (42.3)	
Others	222 (10.0)	40 (10.0)	182 (10.0)	
RAS mutation, yes	275 (32.5)	59 (29.4)	216 (33.5)	0.301
BRAF mutation, yes	79 (9.3)	23 (11.4)	56 (8.7)	0.266
MSI, yes	49 (5.8)	13 (6.5)	36 (5.6)	0.608
Undergoing the targeted therapy, yes	1442 (31.7)	364 (36.8)	1078 (30.3)	< 0.001
Barriers to undergo the targeted therapy				
The physician did not mention it to patients, yes	1253 (40.4)	266 (42.6)	987 (39.8)	0.231
Genetic tests identify tumors that will not respond to targeted therapy, yes	203 (6.5)	40 (6.4)	163 (6.6)	0.944
There is no confidence in the efficacy of these targeted drug treatments, yes	703 (22.7)	102 (16.3)	601 (24.3)	< 0.001
Cannot afford the cost of medical treatment, yes	736 (23.7)	143 (22.9)	593 (23.9)	0.618
Treatments				
Surgery, yes	3823 (83.8)	836 (84.4)	2987 (83.6)	0.612
Endoscopic treatment, yes	141 (3.1)	31 (3.1)	110 (3.1)	0.999
Radiotherapy, yes	1001 (21.9)	266 (26.8)	735 (20.6)	< 0.001
Chemotherapy, yes	3943 (86.4)	906 (91.4)	3037 (85.0)	< 0.001
Immunotherapy, yes	108 (2.4)	24 (2.4)	84 (2.4)	0.992
Out-of-pocket medical expenditure, Chinese Yuan				< 0.001
< 50,000	1147 (25.2)	187 (18.9)	960 (26.9)	
50,000-100,000	1859 (40.8)	365 (36.9)	1494 (41.8)	
100,000-200,000	1040 (22.8)	259 (26.2)	781 (21.9)	
≥ 200,000	514 (11.3)	179 (18.1)	335 (9.4)	
Medical expenditure reimbursement ratio (%)	0.59 (0.18)	0.56 (0.18)	0.59 (0.18)	< 0.001
Annual household income, Chinese Yuan				< 0.001
None	759 (16.7)	106 (10.7)	653 (18.3)	
< 50,000	1855 (40.7)	353 (35.7)	1502 (42.1)	
50,000-100,000	1289 (28.3)	309 (31.3)	980 (27.5)	
100,000-200,000	521 (11.4)	163 (16.5)	358 (10.0)	
≥ 200,000	132 (2.9)	57 (5.8)	75 (2.1)	
Cost of colorectal cancer treatment from the perspective of patients	. ,			0.413
< 50,000	1314 (28.9)	273 (27.7)	1041 (29.2)	
50,000-100,000	1510 (33.2)	319 (32.3)	1191 (33.5)	
100,000-200,000	1103 (24.3)	245 (24.8)	858 (24.1)	
200,000-500,000	524 (11.5)	124 (12.6)	400 (11.2)	
≥ 500,000	96 (2.1)	26 (2.6)	70 (2.0)	

Table 2 (continued)

	Overall	EOCRC, < 50	LOCRC, ≥ 50	Р
	(N=4572)	years (N=991)	years (N=3581)	value
Health insurance				0.005
Urban basic medical insurance	1919 (42.0)	379 (38.2)	1540 (43.0)	
Urban basic medical insurance	981 (21.5)	205 (20.7)	776 (21.7)	
New rural cooperative medical scheme	1552 (33.9)	373 (37.6)	1179 (32.9)	
Other	120 (2.6)	34 (3.4)	86 (2.4)	

Abbreviations EOCRC, Early onset colorectal cancer; LOCRC, Late onset colorectal cancer; CRC, colorectal cancer; MSI, microsatellite instability Values are presented as mean (standard deviations) for continuous variables or n (%) for categorical variables

Table 3 Health-related guality of life in patients with early-onset and late-onset colorectal of

	Number of items	Overall (N=4572)	EOCRC, < 50 years (N=991)	LOCRC, \geq 50 years (N = 3705)	P value
Overall HRQOL*		128.18 (24.72)	127.63 (24.52)	128.33 (24.77)	0.441
FACT-C ¹	36				
Physical well-being	10	31.53 (5.85)	31.25 (6.12)	31.61 (5.77)	0.082
Social/Family well-being	7	22.98 (5.69)	23.04 (5.61)	22.97 (5.71)	0.722
Emotional well-being	5	14.89 (4.33)	14.75 (4.49)	14.92 (4.28)	0.262
Functional well-being	7	14.69 (6.95)	14.85 (6.84)	14.65 (6.98)	0.410
Colorectal cancer subscale	7	17.79 (4.55)	17.90 (4.48)	17.76 (4.57)	0.368
EORTC QLQ-C30	9				
Functional scales and/or it	ems ¹				
Physical	1	3.44 (1.02)	3.60 (0.90)	3.39 (1.05)	< 0.001
Cognitive	1	3.10 (1.00)	3.10 (1.03)	3.11 (0.99)	0.924
Emotional	2	6.24 (1.79)	6.05 (1.91)	6.30 (1.76)	< 0.001
Social	2	5.25 (2.20)	5.04 (2.30)	5.31 (2.17)	0.001
Symptom items [§]					
Fatigue	1	0.89 (1.05)	0.83 (1.03)	0.90 (1.05)	0.051
Sleep disturbance	1	1.15 (1.16)	1.18 (1.19)	1.14 (1.16)	0.349
Financial impacts	1	1.58 (1.24)	1.79 (1.29)	1.52 (1.22)	< 0.001

Values are presented as mean (standard deviations)

*A higher score indicates a better quality of life

¹A higher score indicates a higher level of functioning

[§]A higher score indicates a greater degree of symptoms

speed evaluation and diagnosis of younger patients and potentially improve outcomes.

We also found that patients with EOCRC were more likely to receive gene testing, perioperative chemoradiotherapy, and targeted therapy than those with LOCRC while experiencing similar benefits in HRQOL. Treatment recommendations for patients with EOCRC and LOCRC are consistent with major clinical practice guidelines [20, 21]. However, we found more intensive treatment among young patients. This finding was consistent with previous studies indicating that young patients with CRC received more aggressive surgical treatment, greater resection extent, and more perioperative chemoradiotherapy and targeted therapy than those with LOCRC [7, 22–24]. Nevertheless, whether these aggressive treatments would lead to survival benefits remains controversial. Several studies report a worse prognosis, while others demonstrate equivalent or superior outcomes among younger patients [22, 24-26]. In our study, we found that, despite being more likely to receive chemoradiotherapy and chemotherapy, younger patients had a comparable HRQOL to their older counterparts. This finding can be attributed to two contrasting factors: the inherently more aggressive clinicopathological features and advanced TNM stage of EOCRC, and the more intensive treatment it received. These factors together contributed to similar well-being between the EOCRC and LOCRC groups.

Our study conducted a nationwide survey to gather a representative sample of the Chinese population, which ensures the generalizability of our findings across diverse demographic groups. Additionally, we systematically identified distinctive features of EOCRC by comparing a range of characteristics, including demographics, clinical features, disease knowledge, medical experiences, expenditures, and health-related quality of life. Our study underscored the necessity for tailored screening and treatment strategies for younger CRC patients, offering significant insights that could influence future public health policies and clinical practices in China.

Our study has several limitations. Firstly, we cannot compare the characteristics of EOCRC stratified by predisposing conditions. However, previous studies have indicated that only a minority of EOCRC cases are attributable to hereditary syndromes [2, 27], suggesting that this minority may not significantly impact our findings. Secondly, the self-reported data, including disease knowledge, CRC screening, and HROOL, may be susceptible to recall biases. Nevertheless, we have taken several measures to maintain the accuracy of the data [28, 29]. These included formulating clear and precise questions to reduce variation in comprehension and ensuring the collection of valid and reliable data. Moreover, in-person interviews have been employed to facilitate more accurate recall data. Finally, we did not collect the personal oncological history, family history of diseases and comprehensive comorbidities, which may have influence on HROOL.

Conclusion

Our study found that EOCRC patients, despite having a higher prevalence of widespread metastases and receiving more aggressive treatment and gene testing, still exhibited an HRQOL similar to that of the LOCRC group.

Supplementary Information

The online version contains supplementary material available at https://doi. org/10.1186/s12885-024-12278-7.

Supplementary Material 1

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Author contributions

HWL, HFX, and YL contributed to the conception and design. SKZ and YLQ administratively supported this study. YL, YQZ, XZ, YQY, LBD, YYL, WJW, HLC, LM, JXH, JC, LL, YPF, XFG, CYF, QZ, XHW, and JCD contributed to data curation and data analysis. HWL drafted the manuscript. All authors contributed to the article and approved the submitted version.

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Data availability

Data are available upon reasonable request to the corresponding authors.

Declarations

Ethics approval and consent to participate

This study was approved by the Medical Ethics Committee of Henan Cancer Hospital (No.2019273) and also by the Ethics Committee of all other participating hospitals subsequently. Written informed consent was obtained from each participant.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

- Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. CA Cancer J Clin. 2023;73(1):17–48.
- Patel SG, Karlitz JJ, Yen T, Lieu CH, Boland CR. The rising tide of early-onset colorectal cancer: a comprehensive review of epidemiology, clinical features, biology, risk factors, prevention, and early detection. Lancet Gastroenterol Hepatol. 2022;7(3):262–74.
- 3. Siegel RL, Fedewa SA, Anderson WF et al. Colorectal Cancer Incidence Patterns in the United States, 1974–2013. J Natl Cancer Inst. 2017;109(8).
- Ahnen DJ, Wade SW, Jones WF, et al. The increasing incidence of young-onset colorectal cancer: a call to action. Mayo Clin Proc. 2014;89(2):216–24.
- Lui RN, Tsoi KKF, Ho JMW, et al. Global increasing incidence of Young-Onset Colorectal Cancer Across 5 continents: a Joinpoint Regression Analysis of 1,922,167 cases. Cancer Epidemiol Biomarkers Prev. 2019;28(8):1275–82.

- Cercek A, Chatila WK, Yaeger R, et al. A Comprehensive comparison of early-onset and average-onset colorectal cancers. J Natl Cancer Inst. 2021;113(12):1683–92.
- Gao XH, Li J, Liu LJ, et al. Trends, clinicopathological features, surgical treatment patterns and prognoses of early-onset versus late-onset colorectal cancer: a retrospective cohort study on 34067 patients managed from 2000 to 2021 in a Chinese tertiary center. Int J Surg. 2022;104:106780.
- Chen Y, Chen Z, Huang J, et al. Clinicopathological and molecular characteristics of early-onset vs late-onset colorectal cancer according to tumor location. Int J Clin Oncol. 2022;27(4):749–55.
- Kirzin S, Marisa L, Guimbaud R, et al. Sporadic early-onset colorectal cancer is a specific sub-type of cancer: a morphological, molecular and genetics study. PLoS ONE. 2014;9(8):e103159.
- Watson R, Liu TC, Ruzinova MB. High frequency of KRAS mutation in early onset colorectal adenocarcinoma: implications for pathogenesis. Hum Pathol. 2016;56:163–70.
- Liu Y, Xu HF, Zhang X, et al. Disease knowledge, medical experience, healthrelated quality of life and health-care costs among patients with advanced colorectal cancer in China: protocol for a nationwide multicentre survey. BMJ Open. 2022;12(3):e054403.
- 12. [Chinese Protocol of Diagnosis and Treatment of Colorectal Cancer]. Zhonghua Wai Ke Za Zhi. 2018;56(4):241–58.
- [China guideline for the. Screening, early detection and early treatment of colorectal cancer (2020, Beijing)]. Zhonghua Zhong Liu Za Zhi. 2021;43(1):16–38.
- 14. Cella DF, Tulsky DS, Gray G, et al. The Functional Assessment of Cancer Therapy scale: development and validation of the general measure. J Clin Oncol. 1993;11(3):570–9.
- Wong CK, Lam CL, Law WL, et al. Validity and reliability study on traditional Chinese FACT-C in Chinese patients with colorectal neoplasm. J Eval Clin Pract. 2012;18(6):1186–95.
- Zhao H, Kanda K. Testing psychometric properties of the standard Chinese version of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire 30 (EORTC QLQ-C30). J Epidemiol. 2004;14(6):193–203.
- Cheng JX, Liu BL, Zhang X, et al. The validation of the standard Chinese version of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire 30 (EORTC QLQ-C30) in pre-operative patients with brain tumor in China. BMC Med Res Methodol. 2011;11:56.

- Vuik FER, Nieuwenburg SAV, Nagtegaal ID, Kuipers EJ, Spaander MCW. Clinicopathological characteristics of early onset colorectal cancer. Aliment Pharmacol Ther. 2021;54(11–12):1463–71.
- Chen FW, Sundaram V, Chew TA, Ladabaum U. Advanced-Stage Colorectal Cancer in persons younger than 50 years not Associated with longer duration of symptoms or time to diagnosis. Clin Gastroenterol Hepatol. 2017;15(5):728–e737723.
- 20. Messersmith WA. NCCN guidelines updates: management of metastatic colorectal Cancer. J Natl Compr Canc Netw. 2019;17(55):599–601.
- 21. Dong C, Ding Y, Weng S, et al. Update in version 2021 of CSCO guidelines for colorectal cancer from version 2020. Chin J Cancer Res. 2021;33(3):302–7.
- 22. Kneuertz PJ, Chang GJ, Hu CY, et al. Overtreatment of young adults with colon cancer: more intense treatments with unmatched survival gains. JAMA Surg. 2015;150(5):402–9.
- 23. Zaborowski AM, Abdile A, Adamina M, et al. Characteristics of early-onset vs late-onset colorectal Cancer: a review. JAMA Surg. 2021;156(9):865–74.
- 24. Abdelsattar ZM, Wong SL, Regenbogen SE, Jomaa DM, Hardiman KM, Hendren S. Colorectal cancer outcomes and treatment patterns in patients too young for average-risk screening. Cancer. 2016;122(6):929–34.
- 25. Saraste D, Järås J, Martling A. Population-based analysis of outcomes with early-age colorectal cancer. Br J Surg. 2020;107(3):301–9.
- Zaborowski AM, Murphy B, Creavin B, et al. Clinicopathological features and oncological outcomes of patients with young-onset rectal cancer. Br J Surg. 2020;107(5):606–12.
- 27. Eng C, Jácome AA, Agarwal R, et al. A comprehensive framework for earlyonset colorectal cancer research. Lancet Oncol. 2022;23(3):e116–28.
- Roberts RO, Bergstralh EJ, Schmidt L, Jacobsen SJ. Comparison of selfreported and medical record health care utilization measures. J Clin Epidemiol. 1996;49(9):989–95.
- Brusco NK, Watts JJ. Empirical evidence of recall bias for primary health care visits. BMC Health Serv Res. 2015;15:381.

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