Health-related quality of life in advanced colorectal cancer patients in China: a nationwide hospital-based survey

Yan-Qin Yu,1,2,9, Li Ma3,8, Wen-Jun Wang4, Yu-Qian Zhao5, Hui-Fang Xu6, Ji Cao7, Li Li8, Jin-Qi Hao2, Jing-Ru Gao3, Xiao-Fen Gu9, Yun-Yong Liu10, Juan-Xiu Huang11, Yan-Ping Fan12, Ling-Bin Du13, He-Lu Cao14, Chang-Yan Feng15, Qian Zhu16, Xiao-Hui Wang17, Jing-Chang Du18, Mohamed S. Bangura3, Xi Zhang19, Shao-Kai Zhang6, You-Lin Qiao1,6,20; China Working Group on Colorectal Cancer Survey

Background: Colorectal cancer (CRC) is one of the most common cancers in China, and most CRC patients have already reached an advanced stage by the time of initial diagnosis. Due to the loss of health as a result of cancer, it has consequence on the treatment which may affect the psychophysical and social impairment of CRC patients. These indicators (psychophysical, function and social impairment) affect the health-related quality of life (HRQOL). There are limited studies that focus on advanced CRC patients in...
Introduction

Colorectal cancer (CRC) is a crucial public health issue, ranking third and second in new cases and deaths worldwide in 2020 (1). In 2020, there were an estimated 1.9 million new cases and about 935,000 deaths, accounting for 10% and 9.4% in CRC incidence and death, respectively (1). The incidence rate of CRC in China has displayed an annually increasing trend (2). The latest data from the national cancer registry showed that in 2019, about 110,546 new cases and 53,810 deaths occurred in China, ranking the fourth in incidence and fifth in mortality among all cancers (3). Although the 5-year overall survival (OS) rate has been increasing, the rate for patients with III–IV stage CRC is only about 20% or lower. The majority of patients have developed to an advanced stage at their initial diagnosis, in China, patients have commonly reached stage III or IV by their first diagnosis. Therefore, it is very important to pay attention to the diagnosis, treatment, and quality of life (QOL) of CRC patients in China. QOL is essential in the management of CRC patients as it contributes to the well-being of cancer patients, influences survival and response therapy (4). Factors such as smoking, diet, physical activities and alcohol are linked with QOL. Finding showed that moderate and/or intense physical activities are associated with high physical QOL as a result of decrease level of fatigue and distress (5). Based on above reasons, we carried out this study, which focused on the national multicenter health-related quality of life (HRQOL) of advanced CRC and its influencing factors. As we know, the HRQOL is affected by physical and psychological factors. Patients who have physical symptoms such as abdominal pain, fatigue, diarrhea, flatulence, and altered stool and urinary frequency can be susceptible to deterioration of HRQOL and psychological status, for example, anxiety and depression (6). Although CRC patients frequently experience psychological distress, it can be alleviated or diminished when those patients come to accept their diagnosis and subsequent treatment. Many articles have reported that HRQOL could predict chemotherapy response and toxicity, survival, intervention, diagnosis, and so on (7). But there are limited studies that centered on patients with advanced CRC in China. In order to choose a preferable treatment modality, associated variable factors such as cancer type, social character, and disease stage are important in the assessment of HRQOL (8). However, nation-wide representative data

Methods: This was a cross-sectional, nationwide, hospital-based, and multi-center survey. According to the traditional administrative district definition, we selected 19 hospitals in 7 regions by multi-stage stratified sampling in China. For each eligible CRC patient with stage III or IV in the selected hospitals, socio-demographics, clinical information, and HRQOL were collected based on patients’ self-reporting and/or medical records between March 2020 and March 2021. Patients completed the Functional Assessment of Cancer Therapy Colorectal (FACT-C) plus-traditional Chinese version of the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ)-9.

Results: A total of 4,589 CRC patients (mean age 60.1 years, including 2,730 males and 1,859 females) were included. The total score of HRQOL in population was 128.2±24.70. There were significant differences in the overall score of HRQOL in gender, education level, occupation, region, disease type, and disease stage (P<0.05). The score of HRQOL was better in males, undergraduates and above, unemployed/laid-off, and southwestern and central China. Multivariate analysis showed that education level, occupation, location, number of hospitals visited and treatment methods, and gender were associated with utilities of CRC patients.

Conclusions: The HRQOL is an important outcome measure for CRC patients. The HRQOL scores differed according to socio-demographic and clinical characteristics, and findings of these factors were associated with education level, occupation, region, number of visited and treatment methods, and gender.

Keywords: Health-related quality of life (HRQOL); colorectal cancer (CRC); China

Submitted Jan 21, 2022. Accepted for publication Mar 18, 2022.
doi: 10.21037/atm-22-991

View this article at: https://dx.doi.org/10.21037/atm-22-991
of advanced CRC patients in China has yet to be reported. In this study, we selected the Functional Assessment of Cancer Therapy Colorectal plus-Quality of Life Questionnaire-C9 (FACT-C plus-QLQ-C9) questionnaire (including 46 items), which consisted of all FACT-C items plus 9 items from QLQ-core (C) 30 by using experts’ opinion to establish a HRQOL scale.

The primary purpose of this study is to investigate HRQOL and associated factors of advanced CRC patients in multiple nationwide centers in China. Therefore, we hypothesized that the overall impact has an influence on the QOL of CRC patients in China. We present the following article in accordance with the SURGE reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-991/rc).

Methods
Setting
This was a nationwide, multicenter, hospital-based, and cross-sectional survey conducted in China. According to the traditional Administrative District definition, mainland China was divided into seven different geographic regions (northern, northeastern, northwestern, central, eastern, southern, and southwestern) (9), which involved different levels of CRC burden (10). Multi-stage stratified sampling was adopted to determine the participating hospitals. In stage I, 2 cities of each region were selected by simple random sampling. In stage II, a tertiary cancer hospital and/or a general hospital was selected from each city. A total of 19 hospitals (10 tertiary cancer hospitals and 9 general hospitals) were selected. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board of Henan Cancer Hospital (No. 2019273), and the study was approved by all institutional review boards of the participating hospitals. Informed consent was taken from all the patients.

Population
According to the 8th edition of the American Joint Committee on Cancer (AJCC) tumor-node-metastasis (TNM) staging system (11), we chose CRC patients pathologically diagnosed with stage III or IV from the selected hospitals. The CRC patients were coming from the inpatients, who were recruited by the trained interviewers of the cancer centers (including the department of oncology medicine, oncology surgery, radiotherapy and chemotherapy and anorectal surgery) from the selected hospitals.

All eligible patients provided their informed consent before enrolment. The inclusion criteria were as follows: clinically confirmed stage III or IV CRC patients; aged ≥18 years; without any dementia, language communication disorder and able to understand the investigation procedure. The exclusion criteria were as follows: severe physical, cognitive, and/or verbal impairments that would interfere with a patient’s ability to complete the questionnaire.

Sample size
It was estimated that there were about 400,000 advanced CRC patients in China (12,13). To ensure that the national survey is geographically representative, it was designed that about 1% patients would be enrolled. Considering the non-response rate of 10%, more than 4,445 patients would be enrolled into this survey.

Instruments
Based on the traditional Chinese FACT-C and the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 (14,15), 45 items were selected using experts’ opinion to establish a scale named FACT-C plus QLQ-C9, consisting of 4 function subscales (physical, social or family, emotional, functional). Each positive item is valued on a 5-point Likert scale (not at all =0, a little bit =1, somewhat =2, quite a bit =3, very much =4), while the negative items are valued reversely (not at all =4, a little bit =3, somewhat =2, quite a bit =1, very much =0). The reliability of FACT-C plus QLQ-C9 and 4 scale was high in our study. The Cronbach’s α coefficient of HRQOL, physiological status, emotional status, social or family status, and functional status were 0.80, 0.74, 0.93, 0.86, and 0.85 in our questionnaire. The validity of the questionnaire was tested by calculating the correlation between the score of each item and the score of its field. A large correlation coefficient indicated good content validity. The validity of physiological status, emotional status, and social or family status was good in our study, in which the correlation coefficient was above 0.5. In addition, a pilot survey was conducted in September and October 2019 in 2 hospitals (Henan Cancer Hospital and The First Affiliated Hospital of Baotou Medical College) in order to validate standard operating procedures and the questionnaires.
Procedure

The survey was initiated in March 2020, after all participating centers had obtained ethics committee approval. All patients with III or IV stage provided informed consent before investigation, and the whole investigation process took about 20 min to complete. The survey was conducted face-to-face by trained interviewers. If the patients who have difficulties in reading and completing the scales, trained interviewers help reading and explain, or family members help answer questions. We collected demographic information (birthdate, gender, location, occupational situation, marital status and family members, education, annual household income, and medical insurance type), types of cancer (colon cancer, rectal cancer, and both), disease stage, treatment mode, and other factors (metastasis at the first diagnosis, colonoscopy screening, and number of hospitals visited). During the entire investigation process, we adhered to a strict quality control scheme including data collection, filing, entry, checking, revision, and data locking. Upon completion of the questionnaires, the trained interviewers checked them immediately to avoid missing items and logical errors. If the questionnaires had missing items or obvious logical mistakes (such as missing items and errors), the trained interviewers called the patient to amend and check the information.

Statistical analysis

The original data were entered by two trained research assistants using EpiData software version 3.1 (EpiData, Inc., Redwood City, CA, USA). All the data cleaning and analyses were performed with Statistical Analysis System 9.3 (SAS Institute, Cary, NC, USA). It was considered standard to complete more than 95% in the questionnaires. In the case of missing data, missing value was input. Data were presented as mean ± standard deviation (SD) for continuous variables and percentages (%) for categorical variables. The t-test or variance analysis was performed to compare the dimensions of HRQOL in populations disaggregated by demographic information (gender, age, clinical stage), types of cancer, disease stage, treatment mode, and other factors. We adopted multiple linear regression although its use has been criticized for potentially satisfactory fitting to skewed data, as multiple linear regression was most commonly used in HRQOL studies. Dummy variables were created for multicategory variables, and the dummies for the missing values were entered for each category. Variables with P<0.10 in univariate regression model were entered into the multivariable regression model. Using stepwise regression method, variables with P<0.05 were determined as statistically significant in the final multifactor model. All statistical analyses were conducted with a two-tailed test at a significance level of 0.05.

Results

The sociodemographic information

A total of 4,589 CRC cases were included from 19 hospitals, including 3,036 patients (66.15%) and 1,553 family members of patients (33.85%). The mean age of the participants was 60.1±11.62 years, including 2,730 males and 1,859 females with the ratio of male to female was 1.47:1. The married patients were 94.1%, 29.0% of patients had completed primary school and below, 39.3% were government civil servants & public institution personnel, 98.8% had medical insurance, 53.8% were rectal cancer (Table 1).

The score of HRQOL in advanced CRC patients

The total score of HRQOL in the study population was 128.2±24.70, including the scores of physical, emotional, social or family, and functional factors (53.2±9.57, 33.9±9.05, 23.0±5.68, and 18.1±7.20, respectively). The overall score of HRQOL was statistically significantly different according to gender, education level, occupation, and region (P<0.05), which was better in males, Master’s degree and above, other occupation. There was no statistically significant difference in marriage status, age, and medical insurance types. The score of physical capacity was statistically significant in gender, occupation, and region (P<0.05), which was better in males, unemployed or laid-off, and central. The region and marriage status were statistically significant in score of social or family, and on the contrary in other factors. There were statistically significant differences in emotional and functional factors according to age, gender, education, and region, yet there was no statistically significant difference in marriage, age, medical insurance types, and region, to the exception of education (Table 2).

Comparison of total scores of HRQOL in clinical characters

Regarding the specific clinical characters for CRC, we observed significant differences in metastasis at the first
| Characteristics | Number of patients | Proportion (%) |
|-----------------|-------------------|----------------|
| **Gender**      |                   |                |
| Male            | 2,730             | 59.5           |
| Female          | 1,859             | 40.5           |
| **Marital status** |                 |                |
| Married         | 4,318             | 94.1           |
| Not married/divorced/widowed | 271 | 5.9 |
| **Level of education** |          |                |
| Primary school and below | 1,333 | 29.0 |
| Junior high school | 1,478 | 32.2 |
| High school or Secondary technical school | 1,044 | 22.8 |
| Master degree and above | 734 | 16.0 |
| **Occupation** |                   |                |
| Government civil servants & Public institution personnel | 1,804 | 39.3 |
| Service industry and self-employed | 817 | 17.8 |
| Other occupations | 1,968 | 42.9 |
| **Medical insurance type** |          |                |
| Public health insurance | 4,107 | 98.5 |
| Commercial medical insurance | 13 | 0.3 |
| Self-pay | 51 | 1.2 |
| **Disease type** |                   |                |
| Colon cancer | 2,063 | 45.0 |
| Rectal cancer | 2,470 | 53.8 |
| Both | 55 | 1.2 |
| **Region** |                   |                |
| Eastern | 1,319 | 28.7 |
| Northern | 565 | 12.3 |
| Southern | 672 | 14.6 |
| Central | 690 | 15.0 |
| Northeastern | 364 | 7.9 |
| Southwestern | 652 | 14.2 |
| Northwestern | 327 | 7.1 |
| **Disease stage** |                   |                |
| Stage I/II | 887 | 20.1 |
| Stage III | 1,970 | 44.7 |
| Stage IV | 1,550 | 35.2 |
| Unknown | 182 | 3.9 |
| **Number of hospitals visited*** |          |                |
| 1 | 1,267 | 29.2 |
| 2 | 2,248 | 51.8 |
| ≥3 | 829 | 19.1 |

*, the data was missing. Other occupations including freelance, entrepreneurs, retirees, and unemployed or laid-off. CRC, colorectal cancer; SD, standard derivation.
diagnosis, number of hospital visited, treatment, and targeted drugs were being used. The CRC patients with no metastasis at the first diagnosis, receiving surgery plus chemotherapy, not using targeted drugs, and who visited one hospital had higher scores of HRQOL, and those without such features had worse scores of HRQOL. There were no significant differences in disease type and disease stage. Comparing patients with colon cancer and those with rectal cancer, both patient groups had higher scores of functional and physical factors. Significant differences were observed with respect to functional and physical among CRC patients with stage I/II, stage III, and stage IV. The CRC patients with stage III and IV had higher scores of physical and functional, respectively. Except colonoscopy screening, the score of physical assessments had significant differences in whether or not metastasis was present at the first diagnosis, methods of treatment, whether or not targeted drugs were being used, the number of hospitals visited, which was higher in those with no metastasis at the first diagnosis, receiving surgery + chemotherapy, if they had visited one hospital, and were not using targeted drugs. In addition, we observed significant differences between CRC patients with social/family and emotional factors with respect to the number of hospitals visited and whether or not they were using targeted drugs (Table 3).

Participants who had visited at least 3 hospitals or were using targeted drugs had higher scores of social or familial factors, but it was different from that of emotional factors in those who had visited 1 hospital and were not using targeted drugs. Significant differences were found in function score in methods of treatment among those who were receiving surgery plus chemotherapy higher (Table 3).

The multiple linear regression of HRQOL in advanced CRC patients

There were 9 candidate predictors which showed associations with HRQOL scores in the univariate analyses for advanced CRC patients, with the exception of marriage, age, medical insurance, and disease stage. The HRQOL scores were significantly higher for the CRC patients in the southwestern (β=18.08, P<0.001), women (β=3.66, P<0.001), primary school and below (β=4.28, P<0.001), service industry/migrant workers (β=4.22, P<0.001), visited 1 hospital (β=3.89, P<0.001), and surgery + chemotherapy (β=5.38, P<0.001). Multivariate analysis confirmed 6 of the 9 variables as correlated. Those who had gender, education level, occupation, region, number of hospitals visited, and treatment methods were more likely to have correlated with HRQOL (Table 4).

Discussion

The main purpose of this study was to evaluate the QOL of China’s mainland advanced CRC patients and to assess the influence of gender, age, disease type, disease stage, treatment mode, and other factors on the dimensions of the FACT-C plus QLQ-C9 instruments. To our knowledge, this was the first attempt at a nationwide, multicenter level study in mainland China to elaborate on the related

| Table 2 | The score of HRQOL in advanced CRC patients (x±s, points) |
|---------|----------------------------------------------------------|
| Variables | Physiological status | Social/family status | Emotional status | Functional status | HRQOL |
| Gender | | | | | |
| Male | 54.0±9.31 | 23.0±5.61 | 34.5±8.87 | 18.6±7.18 | 130.0±24.36 |
| Female | 52.2±9.83 | 22.9±5.79 | 32.9±9.23 | 17.5±7.18 | 125.4±24.95 |
| t | 6.04 | 0.80 | 5.70 | 5.06 | 6.16 |
| P value | <0.001 | 0.426 | <0.001 | <0.001 | <0.001 |
| Marital status | | | | | |
| Married | 54.0±9.31 | 23.0±5.62 | 33.8±9.02 | 18.1±7.21 | 128.2±24.72 |
| Not married/divorced/widowed | 52.2±9.83 | 22.3±6.62 | 34.3±9.48 | 18.4±7.01 | 128.2±24.45 |
| t | -0.24 | 2.13 | -0.79 | -0.69 | 0.00 |
| P value | 0.811 | 0.033 | 0.430 | 0.488 | 1.000 |

Table 2 (continued)
Table 2 (continued)

| Variables                  | Physiological status | Social/family status | Emotional status | Functional status | HRQOL  |
|----------------------------|----------------------|----------------------|------------------|-------------------|--------|
| Age (years)                |                      |                      |                  |                   |        |
| <40                        | 53.6±9.63            | 23.0±5.62            | 33.9±9.76        | 18.7±6.99         | 129.1±25.42 |
| 40–59                      | 53.2±9.48            | 23.2±5.63            | 33.5±9.23        | 18.4±7.02         | 128.3±24.08 |
| ≥60                        | 53.2±9.60            | 22.8±5.72            | 34.2±8.81        | 17.9±7.36         | 128.0±25.07 |
| t                          | 0.18                 | 2.57                 | 3.41             | 3.99              | 0.23   |
| P value                    | 0.835                | 0.076                | 0.033            | 0.019             | 0.798  |
| Level of education         |                      |                      |                  |                   |        |
| Primary school and below   | 53.4±9.66            | 22.9±5.51            | 33.6±9.21        | 17.4±7.01         | 127.2±24.82 |
| Junior high school         | 53.1±9.76            | 23.0±5.71            | 34.0±8.88        | 17.8±7.32         | 127.8±25.15 |
| High school or Secondary technical school | 52.9±9.43 | 22.9±5.87 | 33.9±8.93 | 18.4±7.20 | 128.1±24.40 |
| Master's degree and above  | 53.7±9.17            | 23.1±5.67            | 34.1±9.26        | 19.7±7.03         | 130.7±23.88 |
| F                          | 1.13                 | 0.30                 | 0.85             | 18.38             | 3.17   |
| P value                    | 0.337                | 0.828                | 0.467            | <0.001            | 0.023  |
| Occupation                 |                      |                      |                  |                   |        |
| Government servants & public institution | 53.0±9.44 | 23.1±5.77 | 34.2±8.99 | 18.5±7.26 |
| Service industry and self-employed | 52.4±9.47 | 22.6±5.56 | 32.4±9.25 | 17.1±6.82 |
| Other occupation           | 53.8±9.69            | 23.1±5.65            | 34.2±8.97        | 18.2±7.26         | 129.2±24.97 |
| F                          | 7.44                 | 2.79                 | 13.42            | 10.74             | 12.38  |
| P value                    | <0.001               | 0.062                | <0.001           | <0.001            | <0.001 |
| Medical insurance type     |                      |                      |                  |                   |        |
| Public health insurance    | 53.3±9.55            | 23.0±5.64            | 34.0±9.00        | 18.1±7.20         | 128.2±24.77 |
| Commercial medical insurance | 55.5±8.27          | 21.3±5.75            | 35.2±8.60        | 18.1±6.78         | 130.1±24.41 |
| Self-pay                   | 51.6±8.94            | 22.1±5.78            | 32.3±9.70        | 17.1±6.59         | 123.7±22.28 |
| F                          | 1.12                 | 1.23                 | 0.96             | 0.44              | 0.85   |
| P value                    | 0.326                | 0.292                | 0.383            | 0.642             | 0.426  |
| Region                     |                      |                      |                  |                   |        |
| Eastern                    | 52.7±9.95            | 23.2±5.92            | 33.7±9.08        | 17.3±7.45         | 126.9±26.15 |
| Northern                   | 52.2±9.18            | 22.6±6.29            | 33.5±8.30        | 17.8±6.73         | 126.1±23.40 |
| Southern                   | 52.7±9.52            | 22.7±5.35            | 30.1±9.69        | 19.0±6.48         | 124.6±23.29 |
| Central                    | 56.2±8.37            | 22.9±4.84            | 36.2±7.16        | 18.0±6.81         | 132.9±22.08 |
| Northwestern               | 51.4±10.50           | 23.0±5.60            | 33.4±10.36       | 18.4±8.02         | 126.6±28.69 |
| Southwestern               | 55.3±9.05            | 24.3±4.52            | 37.1±8.62        | 20.0±7.51         | 136.7±23.25 |
| Northwestern               | 50.3±8.68            | 20.8±7.21            | 32.1±8.14        | 16.2±6.51         | 119.4±20.33 |
| F                          | 25.57                | 14.81                | 45.68            | 16.28             | 28.36  |
| P value                    | <0.001               | <0.001               | <0.001           | <0.001            | <0.001 |

HRQOL, health-related quality of life.
Table 3 The comparison total scores of HRQOL in clinical characters

| Variables                        | Physiological status | Social/family status | Emotional status | Functional status | HRQOL       |
|----------------------------------|----------------------|----------------------|------------------|-------------------|-------------|
| **Disease type**                 |                      |                      |                  |                   |             |
| Colon cancer                     | 53.6±9.53            | 23.0±6.89            | 34.1±9.06        | 18.4±7.18         | 129.1±24.53|
| Rectal cancer                    | 52.9±9.62            | 23.0±5.51            | 33.7±9.06        | 17.8±7.21         | 127.3±24.89|
| Both                             | 53.9±7.43            | 24.0±5.65            | 33.1±8.52        | 20.0±6.64         | 130.0±21.36|
| F                                | 3.67                 | 0.92                 | 1.00             | 5.53              |             |
| P value                          | 0.025                | 0.400                | 0.388            | 0.004             | 0.056       |
| **Disease stage**                |                      |                      |                  |                   |             |
| Stage I/II                       | 53.7±9.47            | 22.9±5.87            | 34.0±9.06        | 18.5±7.19         | 129.1±24.48|
| Stage III                        | 52.9±9.64            | 23.0±5.55            | 33.7±9.04        | 17.8±7.23         | 127.3±24.96|
| Stage IV                         | 54.3±7.42            | 23.9±5.88            | 32.8±8.42        | 20.0±6.65         | 129.7±21.48|
| F                                | 3.80                 | 0.62                 | 0.84             | 6.23              |             |
| P value                          | 0.022                | 0.539                | 0.432            | 0.002             | 0.053       |
| **Colonoscopy screening**        |                      |                      |                  |                   |             |
| Yes                              | 52.2±9.77            | 22.3±7.53            | 34.7±9.40        | 19.0±8.16         | 128.2±27.17|
| No                               | 53.3±9.56            | 23.0±5.62            | 33.9±9.03        | 18.1±7.17         | 128.2±24.63|
| t                                | −1.16                | −1.34                | 1.05             | 1.40              |             |
| P value                          | 0.247                | 0.179                | 0.294            | 0.161             | 0.996       |
| **Whether metastasis was present at the first diagnosis** | | | | | |
| No                               | 53.8±9.36            | 22.9±5.55            | 34.0±8.73        | 18.2±7.11         | 128.9±24.17|
| Yes                              | 52.3±9.82            | 23.1±5.89            | 33.6±9.56        | 18.1±7.34         | 126.9±25.52|
| t                                | 5.34                 | −0.64                | 1.54             | 0.29              |             |
| P value                          | <0.001               | 0.524                | 0.125            | 0.768             | 0.008       |
| **Number of hospitals visited**  |                      |                      |                  |                   |             |
| 1                                | 53.8±9.84            | 22.8±5.40            | 34.5±8.67        | 18.3±7.32         | 129.3±25.38|
| 2                                | 53.6±9.26            | 23.1±5.72            | 33.9±9.06        | 18.2±7.04         | 128.8±23.96|
| ≥3                               | 51.6±9.79            | 23.3±5.93            | 32.7±9.52        | 17.6±7.25         | 125.1±25.06|
| F                                | 16.38                | 2.32                 | 9.57             | 2.45              | 8.64        |
| P value                          | <0.001               | 0.099                | <0.001           | 0.086             | <0.001      |
| **Treatment**                    |                      |                      |                  |                   |             |
| Surgery                          | 54.0±9.60            | 23.4±5.12            | 34.3±9.07        | 17.6±7.83         | 129.3±25.93|
| Chemotherapy                     | 52.6±9.17            | 22.5±5.98            | 33.8±8.81        | 17.0±6.66         | 126.1±22.67|
| Radiotherapy                     | 52.9±9.97            | 22.2±6.81            | 29.2±11.15       | 15.0±6.80         | 119.3±28.44|
| Surgery + chemotherapy           | 55.0±9.26            | 22.9±5.65            | 34.6±9.00        | 19.2±7.00         | 131.7±24.20|
| Surgery + radiotherapy           | 53.3±8.12            | 24.7±4.92            | 32.6±9.20        | 18.5±6.39         | 129.0±21.81|

Table 3 (continued)
HRQOL scores of advance CRC patients, which are essential for visualizing the overall situation of China, in order to facilitate further updates of the prevention strategy and policy development. Meanwhile, this study further explained the relationships between the demographic and clinical characteristics with HRQOL scores among patients with advanced CRC in China. In our study, using the FACT-C plus QLQ-C9 had good reliability and validity. Cronbach’s α coefficient always assessed the reliability of the questionnaire as suitable, using an acceptable cut-off value of 0.70 (16). Validity of the questionnaire was tested by calculating the correlation between the score of each item and the score of its field. A large correlation coefficient indicates good content validity. A model may be deemed good if its correlation coefficient value was 0.50 or above (16). In this study, the Cronbach’s α coefficient and correlation coefficient were above 0.8 and 0.5, respectively, so the FACT-C plus QLQ-C9 instrument have high scores of reliability and validity.

Our study directly revealed that HRQOL of advanced CRC patients in China was markedly lower than that of the general population (17), but was higher in advanced CRC patients who were male, received less education, unemployed or laid-off, and from southwestern. Comparing males and feminine HRQOL scores, the HRQOL score was higher in males than in females, similar to the findings of the literature reports (18,19). This was shown to be related to their family responsibilities and psychological aspects wherein CRC disease may affect females more than males. The male-to-female-ratio was 1.5, which was aligned with the gender ratio of CRC patients in China. This has been supported in the subscale analysis of functional factors in HRQOL, which was related to good quality of physical status in males. It is noteworthy that emotional status and physical status may affect males more than females, which is distinct from the report by Baider reported (20). Males were always deemed as “strong”, with little communication, sense of embarrassment, and so on, if the males with advanced CRC had more a serious status such as high psychological pressure, leading to reduced tolerance in comparison to females.

In our study, we found that advanced CRC patients with lower education had higher scoring HRQOL than those with higher education, which was similar with functional status in subscale analysis. These results were similar to those of Ratjen et al. (21), which showed that patients with higher education pay more attention to their health, actively cooperate with treatment, and correct erroneous lifestyle and habits, so as to achieve better prognosis and improve their HRQOL (22). Meanwhile, it is suggested that medical staff should provide targeted health education measures and methods according to the educational and cultural level of patients.

This study showed that the HRQOL score of advanced CRC patients with other occupational status was higher than those with government servants or public institution and service industry, and self-employed, which was different from Laghousi et al.’s results (23). The other occupational status population included freelance, entrepreneurs, retirees, self-employed, and unemployed or laid-off, and such people may have pensions, insurance, and more funds, so they heard less pressure than those working in organizations, enterprises, and institutions. This was

| Variables | Physiological status | Social/family status | Emotional status | Functional status | HRQOL |
|-----------|----------------------|----------------------|------------------|------------------|-------|
| Surgery + chemotherapy + radiotherapy | 52.4±9.71 | 23.1±5.26 | 34.0±8.83 | 17.8±7.17 | 127.2±24.48 |
| F         | 5.66                 | 1.31                 | 1.72             | 7.58             | 4.00  |
| P value   | <0.001               | 0.256                | 0.127            | <0.001           | 0.001 |

Using targeted drugs

| Variables | Physiological status | Social/family status | Emotional status | Functional status | HRQOL |
|-----------|----------------------|----------------------|------------------|------------------|-------|
| Yes       | 51.8±9.77            | 23.2±5.96            | 33.3±9.43        | 18.1±6.90        | 126.3±24.40 |
| No        | 53.9±9.41            | 22.9±5.54            | 34.1±8.86        | 18.1±7.33        | 129.0±24.81 |
| t         | −6.61                | 2.05                 | −2.89            | 0.02             | −3.37 |
| P value   | <0.001               | 0.040                | 0.004            | 0.985            | <0.001 |

HRQOL, health-related quality of life.
Table 4 The Multiple linear regression of HRQOL in advanced CRC patients

| Variables                      | Category                                        | β   | SD   | P value |
|--------------------------------|-------------------------------------------------|-----|------|---------|
| Gender                         | Female (reference group = male)                 | −3.66 | 0.76 | <0.001  |
| Level of education             | Reference group = Master’s degree and above     |     |      |         |
|                                | Primary school and below                        | −4.28 | 1.21 | <0.001  |
|                                | Junior high school                              | −3.89 | 1.13 | 0.001   |
|                                | High school or Secondary technical school       | −3.31 | 1.18 | 0.005   |
| Occupation                     | Reference group = other occupation              |     |      |         |
|                                | Government agencies/enterprises/institutions     | −0.63 | 0.85 | 0.461   |
|                                | Service industry/self-employed                  | −4.22 | 1.05 | <0.001  |
| Region                         | Reference group = northwestern                  |     |      |         |
|                                | Eastern                                         | 7.91  | 1.49 | <0.001  |
|                                | Northern                                        | 6.52  | 1.68 | <0.001  |
|                                | Southern                                        | 4.21  | 1.64 | 0.010   |
|                                | Central                                         | 13.02 | 1.64 | <0.001  |
|                                | Northern                                        | 6.52  | 1.68 | <0.001  |
|                                | Southern                                        | 4.21  | 1.64 | 0.010   |
|                                | Central                                         | 13.02 | 1.64 | <0.001  |
|                                | Northeastern                                    | 5.86  | 1.86 | 0.002   |
|                                | Southwestern                                    | 18.08 | 1.63 | <0.001  |
| Disease type                   | Reference group = both                          |     |      |         |
|                                | Colon cancer                                    | −1.42 | 3.44 | 0.679   |
|                                | Rectal cancer                                    | −3.27 | 3.44 | 0.342   |
| Whether or not metastasis was  | Yes (reference group = none)                    | −1.57 | 0.79 | 0.047   |
| present at the time of first   | diagnosis                                       |     |      |         |
| diagnosis                      |                                                 |     |      |         |
| Number of hospitals visited    | Reference group = ≥3                           |     |      |         |
|                                | 1                                               | 3.89  | 1.08 | <0.001  |
|                                | 2                                               | 3.55  | 0.95 | <0.001  |
| Treatment                      | Reference group = surgery + chemotherapy + radiotherapy |     |      |         |
|                                | Surgery                                         | 3.20  | 1.28 | 0.012   |
|                                | Chemotherapy                                     | 0.44  | 1.97 | 0.823   |
|                                | Radiotherapy                                     | −6.90 | 6.02 | 0.252   |
|                                | Surgery + chemotherapy                           | 5.38  | 0.85 | <0.001  |
|                                | Surgery + radiotherapy                           | 2.27  | 4.56 | 0.619   |

HRQOL, health-related quality of life; CRC, colorectal cancer; β, beta parameter; SD, standard deviation.

shown in subscale analysis of social or family status and the majority of patients with public health insurance. There was no significant statistical difference in HRQOL score between medical insurance types. The study have reported that the impact of medicaid insurance on HRQOL is usually related to CRC outcomes such as late diagnosis, high tumor recurrence rate, and low survival rate (24). However, in our study, the majority of patients almost had advanced CRC, with comparable clinical manifestation, treatment mode, and distress.

In order to reflect the HRQOL of advanced CRC patients in mainland China, we recruited more than 4,400
patients from the 7 geographic regions through multi-stage stratified sampling, not only to ensure geographic representativeness and generalization, but also to enable comparison of different regions. From our study, we discovered that southwestern had higher HRQOL than other areas. Notably, emotional status, functional status, and social or family were higher in southwestern, but central was higher in physical status. The possible reason is that there are great regional economic differences and uneven distribution of medical resources.

In a study that did not incorporate analyses of treatment and distress, it was reported that HRQOL was found to vary by disease type, wherein it was higher in patients with urological cancer than those of with CRC (25). Our findings showed that disease type (colon, rectal cancer, and both), disease stages (I/II, III, and IV) did not significantly impact HRQOL, which is inconsistent with Silva et al.’s (26) and Bours’s report (27). The main reason is that patients cannot distinguish the relationship between colon cancer and rectal cancer in mainland China. Due to the distress and complexity of disease, patients with both disease type (colon and rectal) and stage IV had a propensity to worse physical status and better functional status. This is a meaningful research result reflecting that the population has a good implementation effect of three-level prevention. That depends on the difficulty of treatment, method of treatment, cost of treatment, and so on.

At present, the treatment methods of CRC mainly include the following: surgical resection, radiotherapy, chemotherapy, palliative chemotherapy, targeted drug therapy, and immunotherapy (28). The study has confirmed that surgical resection is the main method of treatment for patients with stage II and III CRC (29). The study has also confirmed that surgical resection (laparoscopic resection and colectomy) can improve the HRQOL in patients at 1 month and 3–5 months after operation, and maintain a good HRQOL in patients at 6–8 months after operation (30). Therefore, in order to observe the standardized treatment and prevention of CRC patients in China, we suggest that researchers increase the follow-up duration of HRQOL in patients with advanced CRC. The method of chemotherapy, radiotherapy, and their combination can improve the local disease and survival rate of CRC, but side effects such as physical discomfort, dissatisfaction with life, and psychological pain generally led to diminished HRQOL (31).

In general, patients with CRC using treatment methods such as surgical resection, radiotherapy, systemic chemotherapy, and targeted therapy may experience persistent pain and limited function, which may eventually reduce their QOL (32). The OS rate of patients with CRC who are treated with chemotherapy can significantly increase, for example 5-fluorouracil can improve the survival rate to 30%, but patients have subsequently lower scores in physical, social or family, emotional, and functional status compared to the general population. Previous research has confirmed that type of treatment might be closely related to HRQOL. Our findings showed that patients who underwent surgery plus chemotherapy had higher HRQOL, functional status, and physical status than those of other treatment methods. Our results suggested that patients with cancers requiring chemotherapy and radiotherapy are at greater risk of lower HRQOL scores than those with cancers that do not require other treatment methods. It was associated with treatment effect, treatment cost, patient income, and so on. It is unclear why surgery combined with other treatment measures can yield higher scores of HRQOL than treatment alone, which warrants further research in future (33). Consistent with other research results, the HRQOL of patients who had not used targeted drugs was better and the HRQOL of patients who received targeted drug adjuvant therapy was worse in our study (34). The reason may be the high price of targeted drugs, need for long-term medication, high cost of genetic testing, and the non-reimbursement of medical insurance.

The severity of metastasis at the first diagnosis and number of hospitals visited were also reflected by the HRQOL. In our study, there was a significant difference in HRQOL between patients who had visited one hospital and no metastasis at the first diagnosis. Patients with metastasis at the first diagnosis and had visit at least 3 hospitals needed more treatment methods, treatment cost, and more diagnostic interventions. So that led to lower HRQOL score with heavier disease burden. This result explains that emotional status and physical status impacted highly on HRQOL in patients with just one hospital visited.

The basic variables most often considered in building a CRC model include the following: gender, level of education, occupation, region, number of hospitals visited, and treatment methods. A recent multicenter study in mainland China showed it was higher in the HRQOL of patients with colorectal neoplasms, which was inconsistent with our study (35); however, the sample size of this study was much smaller than that of ours. Meanwhile, our survey was conducted nationwide, which was more representative of the HRQOL in patients with advanced CRC.
**Study strengths and limitations**

This study had some strengths. First, our study helped to fill the gap in HRQOL scores of advanced CRC patients in mainland China, especially those with stage III or IV CRC at the first diagnosis. Second, our study was the first geographic representative study with a large sample of more than 4,400 patients in mainland China. Third, it provides a tool for the HRQOL score, which can be applied to the other cancer types.

This study also had some limitations. The study was cross-sectional; therefore, some biases were inevitable. Additionally, causal relationship between patients’ clinical characteristics and HRQOL scores was not able to be established.

**Conclusions**

The HRQOL is an important outcome indicator for advanced CRC patients. Females patients, primary school and below education level, from the Southwest region, who had visited 1 hospital, and undergone surgery + chemotherapy had higher HRQOL nationwide in China. The scores differed according to sociodemographic and clinical characteristics, and findings of these were associated with education level, occupation, region, number of hospitals visited and treatment methods, and gender. Therefore, the HRQOL should be developed as an assessment method for advanced CRC patients.

**Acknowledgments**

The authors thank the Beijing Love Book Cancer Foundation for originating this clinical epidemiology study of CRC. The authors also thank the local investigators in different cities across the state, including Beijing, Chongqing, Henan (Zhengzhou and Xinxiang), Inner Mongolia (Baotou), Liaoning (Dalian and Shenyang), Zhejiang (Hangzhou), Sichuan (Chengdu), Shandong (Jining), Gansu (Lanzhou), Xinjiang (Ürümqi), Guangxi (Nanning and Wuzhou), and Guangdong (Guangzhou) for the data collection and assistance.

**Funding:** This research was funded by Beijing Love Book Cancer Foundation and Merck Serono Co. Ltd.

**Footnote**

*Reporting Checklist:* The authors have completed the SURGE reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-991/rc

*Data Sharing Statement:* Available at https://atm.amegroups.com/article/view/10.21037/atm-22-991/dss

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-991/coif). All authors report this research was funded by Beijing Love Book Cancer Foundation and Merck Serono Co. Ltd. The authors have no other conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board of Henan Cancer Hospital (No. 2019273), and the study was approved by all institutional review boards of the participating hospitals. Informed consent was taken from all the patients.

**Open Access Statement:** This is an Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: https://creativecommons.org/licenses/by-nc-nd/4.0/.

**References**

1. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin 2021;71:209-49.
2. Song B, Ding C, Chen W, et al. Incidence and mortality of cervical cancer in China, 2013. Chin J Cancer Res 2017;29:471-6.
3. Tian H. China Cancer Registry Annual Report 2019. Beijing: People's Medical Publishing House, 2021.
4. Marventano S, Forjaz M, Grosso G, et al. Health related quality of life in colorectal cancer patients: state of the art. BMC Surg 2013;13 Suppl 2:S15.
5. Buffart LM, Thong MS, Schep G, et al. Self-reported physical activity: its correlates and relationship with health-related quality of life in a large cohort of colorectal cancer survivors. PLoS One 2012;7:e36164.

6. Couwenberg AM, Burbach JPM, Intven MPW, et al. Health-related quality of life in rectal cancer patients undergoing neoadjuvant chemoradiation with delayed surgery versus short-course radiotherapy with immediate surgery: a propensity score-matched cohort study. Acta Oncol 2019;58:407-16.

7. Lee CK, Stockler MR, Coates AS, et al. Self-reported health-related quality of life is an independent predictor of chemotherapy treatment benefit and toxicity in women with advanced breast cancer. Br J Cancer 2010;102:1341-7.

8. Johansson AC, Brink E, Cliffordson C, et al. The function of fatigue and illness perceptions as mediators between self-efficacy and health-related quality of life during the first year after surgery in persons treated for colorectal cancer. J Clin Nurs 2018;27:e1537-48.

9. Zhou M, Wang H, Zeng X, et al. Mortality, morbidity, and risk factors in China and its provinces, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2019;394:1145-58.

10. Yang Y, Han Z, Li X, et al. Epidemiology and risk factors of colorectal cancer in China. Chin J Cancer Res 2020;32:729-41.

11. Weiser MR. AJCC 8th Edition: Colorectal Cancer. Ann Surg Oncol 2018;25:1454-5.

12. Global Cancer Observatory. Available online: https://gco.iarc.fr/today/home

13. Yao HW, Cui L, Zhang W, et al. Annual report of Chinese Colorectal Cancer Surgery Database in 2019: A nationwide registry study. Chinese Journal of Practical Surgery 2020;32:729-41.

14. 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;18:1186-95.

15. 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;14:193-203.

16. Lance C, Butts M, Michels L. The Sources of Four Commonly Reported Cutoff Criteria: What Did They Really Say? Organizational Research Methods 2006;9:202-20.

17. Huang HY, Wang H, Shi JF, et al. Health-related quality of life of patients with colorectal neoplasms in China: A multicenter cross-sectional survey. J Gastroenterol Hepatol 2021;36:1197-207.

18. Momeni M, Ghanbari A, Jokar F, et al. Predictors of quality of life in patients with colorectal cancer in Iran. Indian J Cancer 2014;51:530-6.

19. Pattamatta M, Smeets BJ, Evers SMAA, et al. Quality of life and costs of patients prior to colorectal surgery. Expert Rev Pharmacoecon Outcomes Res 2020;20:193-8.

20. Baider L, Bengel J. Cancer and the spouse: gender-related differences in dealing with health care and illness. Crit Rev Oncol Hematol 2001;40:115-23.

21. Ratjen I, Schafmayer C, Enderle J, et al. Health-related quality of life in long-term survivors of colorectal cancer and its association with all-cause mortality: a German cohort study. BMC Cancer 2018;18:1156.

22. Tran BT, Pham NH, Nguyen TX, et al. Measurement of Health-Related Quality of Life Among Colorectal Cancer Patients Using the Vietnamese Value Set of the EQ-5D-5L. Patient Prefer Adherence 2020;14:2427-37.

23. Laghousi D, Jafari E, Nikbakht H, et al. Gender differences in health-related quality of life among patients with colorectal cancer. J Gastrointest Oncol 2019;10:453-61.

24. McDougall JA, Blair CK, Wiggins CL, et al. Socioeconomic disparities in health-related quality of life among colorectal cancer survivors. J Cancer Surviv 2019;13:459-67.

25. Marco DJT, White VM. The impact of cancer type, treatment, and distress on health-related quality of life: cross-sectional findings from a study of Australian cancer patients. Support Care Cancer 2019;27:3421-9.

26. Silva MMRL, Junior SA, de Aguiar Pastore J, et al. Assessment of quality of life in patients with rectal carcinoma: comparison between sphincter preservation and definitive colostomy. Int J Colorectal Dis 2018;33:1039-45.

27. Bours MJ, van der Linden BW, Winkels RM, et al. Candidate Predictors of Health-Related Quality of Life of Colorectal Cancer Survivors: A Systematic Review. Oncologist 2016;21:433-52.

28. Paika V, Almyroudi A, Tomenson B, et al. Personality variables are associated with colorectal cancer patients' quality of life independent of psychological distress and disease severity. Psychooncology 2010;19:273-82.

29. Dekker E, Tanis PJ, Vleugels JLA, et al. Colorectal cancer. Lancet 2019;394:1467-80.

30. Johdi NA, Sukor NF. Colorectal Cancer Immunotherapy: Options and Strategies. Front Immunol 2020;11:1624.

31. Chan GHJ, Chee CE. Making sense of adjuvant chemotherapy in colorectal cancer. J Gastrointest Oncol 2019;10:1183-92.
32. Eyl RE, Xie K, Koch-Gallenkamp L, et al. Quality of life and physical activity in long-term (≥5 years post-diagnosis) colorectal cancer survivors - systematic review. Health Qual Life Outcomes 2018;16:112.

33. Bours MJ, van der Linden BW, Winkels RM, et al. Candidate Predictors of Health-Related Quality of Life of Colorectal Cancer Survivors: A Systematic Review. Oncologist 2016;21:433-52.

34. Huang W, Yang J, Liu Y, et al. Assessing health-related quality of life of patients with colorectal cancer using EQ-5D-5L: a cross-sectional study in Heilongjiang of China. BMJ Open 2018;8:e022711.

35. Yang J, He YH, Jiang LL, et al. Analysis of the status quo and influencing factors of short-term quality of life after discharge in colorectal cancer patients following enhanced recovery after surgery pathway. Zhonghua Yi Xue Za Zhi 2019; 99:1707-11.

(English Language Editor: J. Jones)