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ORIGINAL RESEARCH

The association between comorbidities and the quality of life among colorectal cancer survivors in the People's Republic of China

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Background: Cancer survivors with certain comorbidities had lower quality of life (QOL). This study was performed to investigate the prevalence of comorbidities and the association between comorbidities and the QOL among Chinese colorectal cancer survivors (CCS).

Methods: A cross-sectional study was conducted among 1,398 CCS between April and July 2013 in Shanghai, People's Republic of China. All the participants were asked to complete a simplified Chinese version of the European Organization for Research and Treatment quality of life version 3 questionnaire and questions on sociodemographic characteristics and comorbidities. In order to mitigate the bias caused by confounding factors, multiple linear regression models were employed to calculate the adjusted means of QOL scores.

Results: The proportion of participants without any comorbidity was only 20.2%. The CCS with comorbidities except hypertension scored significantly lower on the European Organization for Research and Treatment quality of life version 3 questionnaire global health and functioning scales and Functional Assessment of Cancer Therapy-General scales but higher on the European Organization for Research and Treatment quality of life version 3 questionnaire symptom scores, indicating that they had poorer QOL, particularly for cardiovascular, respiratory, digestive, and musculoskeletal diseases.

Conclusion: There exists a significant association between comorbidities and QOL among Chinese CCS, and participants with comorbidities generally reported lower QOL scores. These findings suggested comprehensive care for CCS.

Keywords: colorectal cancer survivors, quality of life, comorbidities, cancer care

Introduction

There were 14.1 million new cancer cases, 8.2 million cancer deaths, and 32.6 million people living with cancer (within 5 years of diagnosis) around the world in 2012. The number of new cancer cases is expected to increase to 24 million by 2035. Colorectal cancer was the third most common cancer with nearly 1.4 million new cases in 2012.[1] In many developing countries, such as the People's Republic of China, the prevalence of colorectal cancer has increased, while mortality rates for colorectal cancer have decreased in recent years.[2–4] The quality of life (QOL) of colorectal cancer survivors (CCS) is undermined by the side effects of cancer and its treatments, and has become a fundamental task of oncological research.[5–8] Assessment of QOL of long-term CCS to monitor and care for both medical and psychological consequences of their cancer treatment and rehabilitation is imperative.

Cancer survivors often have other medical conditions or illnesses, called comorbidities.[9,10] The burden of comorbidity is high, with up to 80% of CCS reporting

at least one comorbidity.[11,12] The most common comorbidities include cardiovascular diseases, musculoskeletal problems, lung or breathing problems, digestive diseases, diabetes mellitus, and depression.[12–14]

There are an increasing number of studies demonstrating that comorbidities have an additive impact on QOL among patients with several chronic diseases. For example, a higher number in comorbidities is associated with the deterioration of QOL,[15–17] and different comorbidities have different impacts on QOL.[18–20] And, several studies also found that comorbidities were associated with poorer QOL among cancer patients in countries other than the People's Republic of China.[21,22] Despite the prevalence and burden of colorectal cancer in patients, to our knowledge there is little information regarding the associations between comorbidities and QOL among CCS. This is particularly true for CCS who have survived beyond the initial treatment period. QOL information on CCS is important if one wishes to evaluate the impact of the disease and its treatments beyond survival, and to understand how QOL is influenced by comorbidities. Understanding these factors can help the medical providers to better identify those who may be at greater risk of diminished functioning and improve targeted delivery of cancer management programs.

In this study, we investigated the prevalence of comorbidities in CCS and assessed whether comorbidities were negatively associated with QOL among CCS in the People's Republic of China. A better understanding of the association between comorbidities and QOL among CCS forms the basis for improving their cancer care and QOL.

Methods
Recruitments
Between April and July 2013, participants were recruited from 17 multicommunity cancer rehabilitation centers, all of which were affiliated to Shanghai Cancer Rehabilitation Club (SCRC), Shanghai, People's Republic of China, a nongovernment organization serving cancer survivors exclusively. This self-help support group aiming at improving the survivors' QOL regularly offers rehabilitation activities, including physical exercise, relaxation training, counseling, psychotherapy, and a variety of leisure activities.[23] The criteria for study enrollment are: 1) being clinically diagnosed with primary colorectal cancer; 2) being able to read, write, and speak in Chinese; and 3) volunteering to participate in this study. A total of 2,102 CCS had registered in the SCRC by the end of 2012. All members of the SCRC who intended to continue to participate in the SCRC were

required to register annually, including both former and new members. The survey invitations were sent through short text messages and/or phone calls to all the 2,102 CCS. Among all these CCS, 169 were unable to be reached because of death, migration, or refusing to respond; 554 failed to participate in the survey either because they had no time or because their health status or literacy ability was too poor. Finally, 1,398 participated in this survey and formed our final sample. Ethical approval to conduct this study was granted by the Medical Research Ethics Committee of the School of Public Health, Fudan University (protocol number RB #2013-04-0450). A written informed consent was obtained from each participant.

Instruments
Demographic characteristics
The demographic characteristics included age, sex, body mass index, years since diagnosis, marital status, the highest educational level achieved, and monthly household income per capita.

Comorbidities
Participants were asked to indicate either "yes" or "no" on a list of comorbidities, including hypertension; diabetes mellitus; and cardiovascular, respiratory, digestive, and musculoskeletal diseases.

QOL measurements
The QOL was measured by the simplified Chinese version of the European Organization for Research and Treatment quality of life version 3 questionnaire (EORTC QLQ-C30).[24] The EORTC QLQ-C30 core questionnaire contains five functional scales (physical, role, cognitive, emotional, and social), three symptom scales (fatigue, pain, and nausea and vomiting), a global health scale, a number of single items assessing additional symptoms commonly reported by cancer patients (dyspnea, appetite loss, insomnia, constipation, and diarrhea), and the financial impact of the disease. For most items, four response categories from 1 (not at all) to 4 (very much) are employed; two items (overall health and overall QOL) have response categories ranging from 1 to 7. The scoring systems are organized such that a high scale score represents a higher response level. Thus, a high score for a functional scale, the global health status, or overall QOL represents a high or healthy status or a high QOL; however, a high score for the symptom scales represents a high level of symptomatology or problems. The scoring of the EORTC QLQ-C30 items was performed according to the EORTC

scoring manual. In this study, the raw EORTC QLQ-C30 scores were transformed to scores ranging from 0 to 100.[25]

EORTC QLQ-C30 scales have shown good reliability in several different language versions as well as in simplified Chinese versions.[26–29] In a study among Chinese cancer patients in which the reliabilities (as measured by Cronbach's alpha) of the scales were assessed on the first and second day of their being hospitalized, the results indicated that the alpha coefficients for all domains were >0.7, except for cognitive functioning (0.49). The test–retest reliability coefficients for most domains were >0.80, except for appetite loss (0.77) and diarrhea (0.75).[29]

Statistical analysis

Standard statistical methods were used to examine potential differences in covariates by one-way analysis of variance for continuous variables followed by Bonferroni post hoc tests. Comorbidity was defined in the statistical analyses as a dichotomous variable (yes/no). Multiple linear regression models were used to compute regression coefficients (β) and associated 95% confidence intervals as estimates of the mean difference of QOL scores associated with the presence or absence of comorbidities, adjusting for potential confounding variables. The following potentially confounding variables were included in all regression models: age (continuous), body mass index (continuous), years since diagnosis (continuous), household income (continuous), education (less than junior high school, junior high school, or above junior high school), and current marital status (married/living with partner or divorced/widowed/separated/single). Tests for trend were performed by entering the categorical variables as continuous parameters in the model. Linear regression was applied to each of the variables measured in EORTC QLQ-C30. Comorbidity and other diseases (hypertension, diabetes mellitus, etc.) were not included in one model. Statistical tests were based on a two-tailed probability with a significance level of 0.05. Statistical analyses were performed using the Statistical Package for the Social Sciences for Windows (Version 21.0; IBM Corporation, Armonk, NY, USA).

Results
The characteristics of the study sample

The sociodemographic characteristics of the 1,398 participants (670 males and 728 females) and the prevalence of comorbidities in CCS are summarized in Table 1. The mean age was 64.5 years and average years since diagnosis were 8.6 years. Only one-fifth (20.2%) of CCS reported no comorbidities. The most common comorbidity among CCS was

Table 1 Summary statistics of 1,398 colorectal cancer survivors

Variables	Number (%)
Age (years)	
<50	45 (3.2)
50–59	343 (24.5)
60–69	649 (46.4)
≥70	361 (25.8)
Sex	
Male	670 (47.9)
Female	728 (52.1)
Body mass index (BMI, kg/m^2)	
<18.5	169 (12.1)
≤18–<25	735 (52.6)
≤25–<30	366 (26.2)
≥30	128 (9.2)
Years since diagnosis	8.6±7.0
Marital status	
Divorced/widowed/separated/single	158 (11.3)
Married/with partner	1,240 (88.7)
Education	
Primary school	144 (10.3)
Middle school or vocational school	1,005 (71.9)
Junior college or above	249 (17.8)
Monthly household income per capita (¥)	
Under 2,000	348 (24.9)
2,000–4,000	805 (57.6)
Over 4,000	245 (17.5)
Number of comorbidities	
0	283 (20.2)
1	311 (22.2)
2	277 (19.8)
≥3	527 (37.7)
Comorbidities	
Hypertension	538 (38.5)
Diabetes	250 (17.9)
Cardiovascular	360 (25.8)
Respiratory diseases	169 (12.1)
Digestive diseases	723 (51.7)
Musculoskeletal diseases	409 (29.3)

digestive diseases (51.7%). Other comorbidities are listed according to their prevalence as follows: hypertension (38.5%), diabetes mellitus (17.9%), heart and cardiovascular diseases (25.8%), respiratory diseases (12.1%), and musculoskeletal diseases (29.3%).

The association between comorbidities and adjusted scores of QOL

The association between comorbidities and adjusted scores of QOL is presented in Table 2. The results of multiple linear regression models showed that the participants with self-reported comorbidities generally reported lower scores for most EORTC QLQ-C30 scales when compared to the participants without these comorbidities. The influences of heart

Table 2 The association between comorbidities and adjusted scores of QOL among colorectal cancer patients

	With Comorbidity, n=1,115 (without comorbidity, n=283)	With HPT, n=538 (without HPT, n=860)	With DM, n=250 (without DM, n=1,148)	With HD, n=360 (without HD, n=1,038)	With RD, n=169 (without RD, n=1,229)	With DD, n=723 (without DD, n=675)	With MD, n=409 (without MD, n=989)
EORTC QLQ-C30							
PF	−4.6 (81.9)***	−1.4 (81.9)	−2.9 (80.4)*	−6.1 (78.1)***	−8.4 (75.3)***	−4.3 (80.8)***	−7.6 (77.4)***
RF	−3.7 (89.0)*	−1.0 (89.1)	−2.7 (87.5)	−5.5 (85.5)***	−5.7 (84.7)**	−3.7 (88.0)**	−5.1 (86.1)***
CF	−5.6 (84.5)***	−2.1 (84.2)	−3.6 (82.6)*	−6.0 (81.0)***	−11.4 (75.5)***	−4.4 (83.6)***	−6.9 (80.7)***
EF	−5.8 (78.5)***	−0.9 (79.0)	−3.9 (76.4)**	−6.7 (74.5)***	−10.2 (70.6)***	−5.1 (77.3)***	−8.7 (73.5)***
SF	−5.9 (77.5)**	−0.2 (78.5)	−2.3 (76.8)	−6.6 (73.6)***	−15.1 (65.3)***	−6.8 (75.6)***	−8.6 (72.6)***
QL	−7.1 (60.6)**	−5.3 (58.7)**	−4.6 (58.3)*	−9.2 (55.0)***	−16.5 (47.5)***	−5.9 (59.3)***	−8.2 (56.2)***
FA	11.0 (29.8)***	1.5 (28.7)	5.0 (31.8)**	8.1 (33.9)***	14.0 (40.1)***	8.8 (31.7)***	8.6 (33.8)***
NV	1.1 (3.2)	0.3 (3.2)	1.6 (4.3)	1.3 (4.0)	5.0 (7.4)***	1.0 (3.5)	1.4 (4.0)
PA	7.8 (17.4)***	1.7 (17.0)	4.1 (19.2)**	9.3 (23.0)***	12.0 (26.5)***	5.3 (18.3)***	13.7 (25.5)***
DY	6.3 (15.8)***	3.0 (16.5)*	2.7 (16.8)	8.9 (21.4)***	16.3 (29.0)***	4.6 (16.7)***	7.6 (20.0)***
SL	4.5 (18.7)*	0.5 (18.2)	2.4 (19.8)	4.8 (21.5)**	8.0 (24.9)**	6.3 (20.7)***	5.9 (22.0)**
AP	3.4 (10.9)*	1.7 (11.3)	3.1 (12.8)*	5.6 (14.5)***	9.1 (18.3)***	3.2 (11.7)*	6.4 (14.7)***
CO	8.0 (15.8)***	0.2 (14.5)	2.3 (16.2)	3.7 (17.1)*	7.5 (20.9)**	7.7 (17.8)***	5.7 (18.3)***
DI	5.6 (12.7)**	2.9 (13.4)*	3.6 (14.5)*	5.4 (15.7)***	10.9 (21.2)***	6.0 (14.3)***	4.4 (14.7)**
FI	4.3 (30.4)	0.7 (30.0)	1.3 (30.7)	4.6 (33.1)*	12.2 (40.3)***	4.7 (31.7)*	7.1 (34.6)***

Notes: *$P<0.05$, **$P<0.01$, ***$P<0.001$. Data presented as difference in mean score of QOL between CCS with and without comorbidities (mean score of QOL among CCS without comorbidities). Multiple linear regression, adjusted for influence of sex, age, BMI, education, household income, time after diagnosis.

Abbreviations: AP, appetite loss; BMI, body mass index; CCS, colorectal cancer survivors; CF, cognitive functioning; CO, constipation; DD, digestive diseases; DI, diarrhea; DM, diabetes mellitus; DY, dyspnea; EF, emotional functioning; EORTC QLQ-C30, European Organization for Research and Treatment quality of life version 3 questionnaire; FA, fatigue; FI, financial difficulties; HD, heart and cardiovascular diseases; HPT, hypertension; MD, musculoskeletal diseases; NV, nausea and vomiting; PA, pain; PF, physical functioning; QL, global health; QOL, quality of life; RD, respiratory diseases; RF, role functioning; SF, social functioning; SL, insomnia.

and cardiovascular diseases, respiratory diseases, digestive diseases, and musculoskeletal diseases on EORTC QLQ-C30 scores were of a similar magnitude and were larger than the influence of hypertension or diabetes mellitus.

Discussion

Based on our data, comorbidities, including hypertension, diabetes mellitus, heart and cardiovascular diseases, and respiratory, digestive, and musculoskeletal diseases, were quite common among CCS. This study showed that Chinese CCS with certain comorbidities such as cardiovascular, respiratory, digestive, and musculoskeletal diseases had lower QOL.

Previous studies suggested that age, income, educational level, marital status, and other variables had influence on QOL in cancer survivors.[30,31] The main purpose of this study was to understand the impact of comorbidities on QOL; therefore, we used multiple linear regression models to control the effects of sociodemographic characteristics.

Cancer survivors with comorbidities have different clinical and health care needs than those without comorbidities. Moreover, cancer survivors tend to have more than one comorbidity.[32,33] In our study, ~80% of CCS had at least one comorbidity, and nearly 40% had more than three comorbidities. Noticeably, more than half of the CCS had digestive diseases, which was the most common comorbid condition in our sample. Therefore, in order to enhance QOL of CCS, more attention should be paid to their comorbidities, especially digestive disorders. It is crucial to implement a comprehensive management program for chronic diseases and address the overall issues rather than apply stopgap and piecemeal solutions.

Chronic diseases are the major causes of death and disability worldwide. Chronic diseases, such as cancer, heart disease, stroke, diabetes mellitus, and respiratory diseases, share major risk factors in the field of unhealthy lifestyles, including tobacco use, unhealthy diet, physical inactivity, and lack of access to preventive care that are beyond genetics and social inequalities. With rapid modernization in the People's Republic of China, changes in people's lifestyle have been blamed for the increase in the prevalence of colorectal cancer.[34] High caloric intake and physical inactivity are suspected to be the associated factors of colorectal disease and known to often result in many other comorbidities, for example, diabetes mellitus, hypertension, dyslipidemia, coronary heart disease, gallbladder disease, arthritis, and constipation.[35–38] Our previous studies have also clearly indicated that the comorbidities and unhealthy lifestyle have negative influence on QOL among

cancer survivors.[39,40] The CCS with or without comorbidities should build a healthier lifestyle.

The association between the comorbidities and colorectal cancer challenges the old oncology treatment paradigms that solely focus on the disease itself. Collaborative chronic disease management models emphasize the continuity of long-term care and a good relationship between the patient and the provider, in which the patient is empowered to take an active role in their ongoing care such as making lifestyle changes;[41,42] such models may be particularly appropriate to improve the QOL of cancer survivors.

Admittedly, there were some limitations in our study. First, all participants were recruited from one Cancer Rehabilitation Club, even though it has ~13,500 cancer survivor members from all 17 districts in Shanghai. We acknowledge that selection bias may affect the study results. Second, the information on cancer staging is not available, so we are unable to examine the association between cancer staging and QOL. Future study should collect information on cancer staging and conduct analysis to determine the relationship between cancer staging and QOL. Finally, the validity of self-reported comorbidities could be questionable.[43] Participants were asked to answer the questions related to morbidities based on clinical diagnosis. These self-report comorbidity items could be a viable tool to collect comorbidity data.[44] However, we still lack a mechanism to double check the correctness of answers. In addition, we did not report about those who had comorbidities, how many were treated, and how well the disease was controlled. Other issues were that cancer staging and the type of treatment received were not controlled in the model. The internal validity may be affected to a certain extent.

Conclusion

There exists an association between comorbidities and QOL among Chinese CCS, and participants with comorbidities generally reported lower QOL scores. These findings underscore the importance of collaborative chronic disease management for CCS.

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Disclosure

The authors report no conflicts of interest in this work.

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