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Quality of life and the negative impact of comorbidities in long-term colorectal cancer survivors: a population-based comparison

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Abstract

Purpose Colorectal cancer (CRC) is the third most common cancer in the USA. The objective of this study was to compare quality of life (QoL) across long-term colorectal cancer survivors and unaffected matched controls while adjusting for comorbidities.

Methods The National Cancer Institute (NCI)-funded Colon Cancer Family Registry (CCFR) was used to randomly select and recruit CRC survivors (≥ 5 years from diagnosis) and matched controls for a cross-sectional survey. Nine geographically diverse sites in the USA from the CCFR participated in the study. Telephone interviews were conducted using computer-assisted methods to assess QoL.

Results A total of 403 cases and 401 controls were included in the final sample. Unadjusted comparison revealed no significant difference between CRC survivors and controls with respect to measures of fatigue, social, emotional, functional, and physical well-being. Multivariate logistic regression revealed that case status had a significant negative influence on colorectal cancer-specific QoL measures. Higher comorbidity indices had a significant negative influence on overall QoL regardless of case status.

Conclusions Quality of life among long-term CRC survivors is similar to control subjects, with the exception of worse CRC-specific QoL measures. Higher comorbidity indices were independently associated with poor QoL for both cases and controls.

Implications for Cancer Survivors Survivors and healthcare providers should be aware that long-term QoL is comparable to the general population; however, there is potential that digestive tract-specific issues may persist.

Keywords Long-term survivorship · Colorectal cancer · Colon cancer · Quality of life · Global quality of life

Introduction

Colorectal cancer (CRC) is the third most commonly diagnosed cancer in the USA [1, 2]. Estimates suggest that more than 140,000 adults are diagnosed annually [2]. Mortality has sharply declined over the past three decades due to improvements in treatment, changing risk factor patterns, and early detection via screening, and continues to decline by an average of 2.5% per year [1, 3]. However, the incidence of colorectal cancer among adults younger than age 50 years has been increasing [1]. Currently, CRC has a relative 5-year survival rate of 65% [1, 2] and 10-year survival rate of 58% [1] accounting for over one million survivors in the USA [1, 4].

Over the past few decades, quality of life (QoL) assessments have emerged as a valuable indicator of healthcare outcomes [5–11]. Extensive research has been done to create and validate general and disease-specific questionnaires that quantify QoL as a measurable outcome that may be used to guide investigations pertaining to novel therapeutic interventions and cancer survivorship programs [11, 12]. Literature concerning quality of life among CRC survivors is often centered around outcomes within the 5-year post-diagnosis period [13–16]. Of the studies examining the impact of colorectal cancer on QoL among long-term CRC survivors [5, 17–21], few include comparable controls or assess the influence of comorbidities on QoL.

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Data from studies of long-term CRC survivors suggest that QoL is similar to the general population, with the exception of worse bowel-related symptoms [5, 17–20]. Most survivorship support programs focus on the immediate post-treatment period. Examination of QoL among long-term CRC survivors is necessary to identify potentially modifiable factors relating to physical, emotional, and social well-being. The objective of this study was to compare quality of life across long-term colorectal cancer survivors (≥ 5 years from diagnosis) and unaffected frequency matched controls while adjusting for comorbidities as measured by the Charlson Comorbidity Index.

Methods

Ethics statement

This study was approved by the Colorado Multiple Institutional Review Board.

Recruitment

This project utilized the infrastructure of the NCI-funded Colon Cancer Family Registry (CCFR) to randomly select and recruit colorectal cancer cases and control subjects to participate in a cross-sectional survey. Nine centers/universities from the CCFR participated in the study: Mayo Clinic, Fred Hutchinson Cancer Research Center, and the Universities of Arizona, Colorado, Hawaii, Minnesota, North Carolina, Southern California, and Dartmouth University. Cases were diagnosed from 1998 to 2007 and thus were more than 5 years from diagnosis when interviews were completed in 2011 to 2012. Control subjects were either unaffected family members of cases who were not selected, or population-based. Controls were frequency matched to cases by age category, gender, and time of enrollment.

Data was collected by trained personnel via computer-assisted telephone interviewing (CATI) conducted at the NCI-funded Survey Research Core at the University of Colorado Comprehensive Cancer Center. Standard CATI protocol allowed for three attempts for recruitment purposes and a maximum of 12 attempts to reach consented subjects. Those who had unverified contact information were deceased or did not give the CCFR permission to be contacted by the project team at the University of Colorado were deemed ineligible for participation.

Measures

Outcomes were measured using validated tools including the Functional Assessment of Cancer Therapy-General (FACT-G) [22], Functional Assessment of Cancer Therapy-Colorectal Cancer (FACT-C) [23], and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) [24]. The FACT-G is a 28-item questionnaire used to assess the domains of physical, social/family, emotional, and functional well-being [22]. The FACIT-F (13 items) [23] and FACT-C (10 items) [24] address the domain of fatigue and colorectal cancer–specific symptoms, respectively. The FACT-C specifically addresses issues including abdominal cramps, weight loss, incontinence, digestion, appetite, satisfaction with physical appearance, and if applicable, ostomy-related embarrassment and difficulty [24]. All FACT-G, FACT-C, and FACIT-F responses are documented on a Likert scale [7].

Comorbidities were measured using the Charlson Comorbidity Index as calculated by subject-reported health status [25] obtained via telephone interview. The Charlson Comorbidity Index was calculated without cancer items to allow for comparison with control subjects. Covariates including age, gender, and education were gathered from the CCFR database for consenting subjects; similarly, information regarding stage, date of diagnosis, and other relevant disease status information was gathered from the CCFR database for past diagnoses and re-assessed for new disease during the current interview.

Response rates

Of the 1374 CRC cases identified via CCFR, 941 were eligible for recruitment (Fig. 1); of this group, 495 individuals consented to participate (response rate = 52.6%). Of the 1809 control subjects identified via CCFR, 1030 were eligible for recruitment; of this group, 436 individuals consented to participate (response rate = 42.3%). The survey completion rate was 90.9% for cases ($n = 450$) and 92% for controls ($n = 401$).

Statistical analysis

Cases with metastatic disease ($n = 15$), recurrence ($n = 28$), or ongoing treatment ($n = 4$) were excluded from analysis. The race/ethnicity variable was recoded into two categories, "Non-Hispanic White" and "Other," for ease of analysis. Outcomes were defined as FACT continuous scores (subscales and total). Questions asked only of cases were eliminated from analysis; therefore, scores were standardized on a scale of 0–100 for comparability. Univariate comparisons were performed using t test or chi-square analysis as appropriate. Multivariate logistic regression analysis was performed to explore the relationship between prior CRC diagnosis and QoL. All statistical analyses were performed using the SAS software version 9.3 (SAS Institute Inc., Cary, NC, USA).

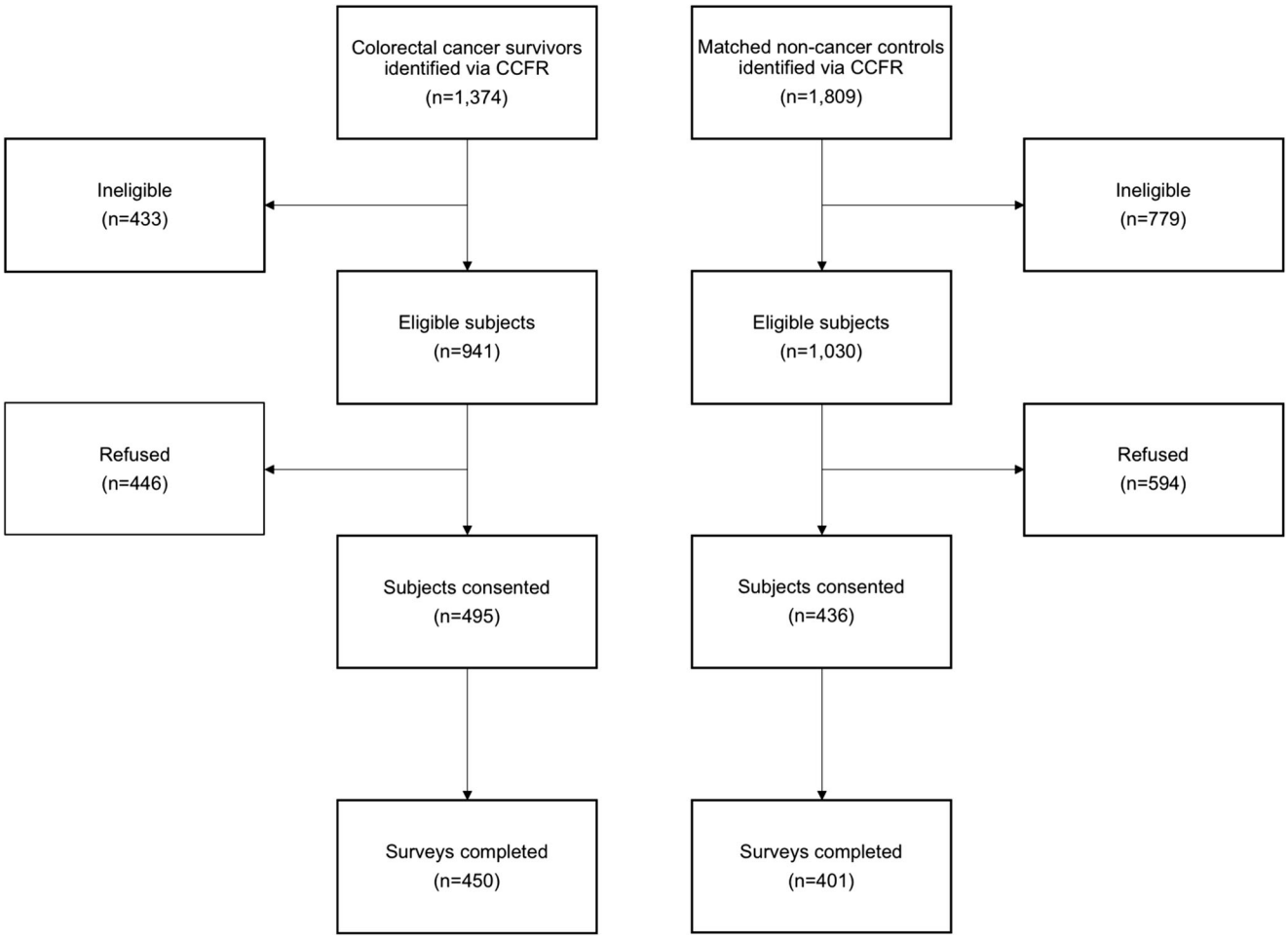

Fig. 1 Flowchart detailing recruitment and inclusion

Results

A total of 403 cases and 401 controls were included in the final sample. Cases were a median of 9.9 years from diagnosis (IQR 8, 11.9 years). There was no significant difference with respect to age, sex, relationship status, highest level of education attained, insurance status, or Charlson Comorbidity Index categorization across the two groups (Table 1). There were more non-Hispanic white individuals among the cases (79.6% vs 69.6%, $p = 0.001$). Of the 82 cases whose race/ethnicity was coded as "Other" for analysis, there were 14 Asian individuals, 17 Black individuals, 10 Hispanic individuals, three individuals whose race/ethnicity did not fit within the aforementioned categories, and 38 individuals with missing data. Of the 122 controls whose race/ethnicity was coded as "Other" for analysis, there were 11 Asian individuals, 13 Black individuals, one Hispanic individual, four individuals whose race/ethnicity did not fit within the aforementioned categories, and 93 individuals with missing data.

Univariate analysis of the FACT domains revealed no significant difference in Physical, Social, Emotional, Functional, General, and Fatigue mean assessment scores across the two groups (Table 2). The General assessment is a composite score of the Physical, Social, Emotional, and Functional assessments. There was no significant difference in the General + Fatigue and General + Colorectal Cancer mean assessment scores across the two groups. The only FACT domain significantly influenced by case status was the Colorectal Cancer assessment (case-control difference − 3.48 (95% CI, − 5.23, − 1.73), $p < 0.001$).

Multivariate logistic regression revealed that case status (OR 0.06 (95% CI 0.01, 0.36), $p = 0.002$) and higher Charlson Comorbidity Index scores have a significant negative influence on FACT–Colorectal Cancer scores (Table 3). A second multivariate model was built to determine whether case status continued to exert a negative influence on QoL as represented by FACT–General + Colorectal Cancer scores. Case status did not significantly influence FACT–General + Colorectal Cancer scores; however, higher Charlson Comorbidity Index scores continued to have a strong, significant negative impact on quality of life (Table 3). Other factors influencing FACT–General + Colorectal Cancer scores

Table 1 Demographic summary

	Cases ($n = 403$) n (%)	Controls ($n = 401$) n (%)	p value
Age (years)			
< 50	53 (13.2)	66 (16.5)	0.222
50–64	187 (46.4)	164 (40.9)	0.133
≥ 65	163 (40.4)	163 (40.6)	0.505
Missing	-	8 (2)	-
Sex			
Male	190 (47.2)	184 (45.9)	0.777
Female	213 (52.8)	217 (54.1)	0.777
Race			
White	321 (79.6)	279 (69.6)	0.001*
Other	82 (20.4)	122 (30.4)	0.001*
Relationship status			
Partner	299 (74.2)	318 (79.4)	0.102
Single	104 (25.8)	82 (20.4)	0.102
Missing	-	1 (0.2)	-
Education			
≤ High school	82 (20.3)	61 (15.2)	0.07
Some college	117 (29)	112 (27.9)	0.791
≥ College	204 (50.6)	227 (56.6)	0.103
Missing	-	1 (0.2)	-
Insurance			
None	20 (5)	13 (3.3)	0.292
Public	119 (29.5)	130 (32.4)	0.417
Private	264 (65.5)	258 (64.3)	0.791
Charlson Comorbidity Index			
0	258 (64)	246 (61.4)	0.475
1	70 (17.4)	63 (15.7)	0.590
≥ 2	75 (18.6)	92 (22.9)	0.153

included higher education (OR 23.10 (95% CI 2.29, 233.41), $p = 0.008$) and public insurance (OR 0.06 (95% CI 0.006, 0.485)).

Discussion

To our knowledge, this is the largest multisite study comparing QoL among long-term CRC survivors (≥ 5 years from diagnosis) and matched control subjects. Most of the 403 CRC survivors included in our final sample were approximately 10 years from initial diagnosis, and all subjects were recruited from geographically heterogeneous locations in the USA. We found that overall QoL for long-term CRC survivors is comparable to control subjects, as indicated by similar scores on the FACT-G assessment. However, CRC-specific QoL measures primarily related to digestive function were worse among survivors. Higher Charlson Comorbidity Index scores had a significant negative impact on overall QoL irrespective of prior cancer diagnosis.

There is extensive literature addressing quality of life among CRC survivors. The effect of age on psychosocial distress among CRC survivors is controversial [26]; certain studies have demonstrated that younger adult CRC survivors experience higher levels of psychosocial distress compared with their older counterparts [15], whereas other investigations concluded that older age is associated with poor psychosocial functioning [18]. Investigations that included comparisons with population-based controls reported that CRC survivors surveyed within 5 years after diagnosis were more likely to report poor physical, social, and digestive function [18, 19]. Individuals assessed at 1 year after CRC diagnosis reported worse physical, role, cognitive, and global health functioning compared with population controls; deficits in emotional and social functioning, as well as physical symptoms relating to fatigue and digestive impairment, contributed extensively to impaired QoL [14].

While most QoL studies were performed using cross-sectional methodology, there are a few notable exceptions. Chambers et al. conducted a study evaluating baseline QoL (at 5 months post-diagnosis) and long-term QoL (at 5 years post-diagnosis) for a cohort of CRC survivors diagnosed between January 2003 and December 2004 [13]. The authors

Table 2 Mean standardized functional assessment scores by case-control status

	Cases ($n = 403$)	Controls ($n = 401$)	Case-control difference (95% CI)	p value
Physical	87.46 ± 14	88.75 ± 11.31	− 1.29 (− 3.06, 0.47)	0.150
Social	77.38 ± 17.78	75.96 ± 18.37	1.42 (− 1.09, 3.93)	0.266
Emotional	84.37 ± 16.64	83.19 ± 13.89	1.18 (− 0.94, 3.30)	0.276
Functional	79.54 ± 18.73	77.51 ± 17.42	2.03 (− 0.47, 4.54)	0.111
General	82.63 ± 12.87	81.86 ± 11.11	0.77 (− 0.90, 2.43)	0.367
Fatigue	83.04 ± 16.78	82.79 ± 15.09	0.25 (− 1.96, 2.46)	0.826
Colorectal cancer	81.52 ± 14.12	85 ± 10.95	− 3.48 (− 5.23, −1.73)	< 0.001*
General + fatigue	82.77 ± 13.39	82.19 ± 11.59	0.59 (− 1.15, 2.32)	0.508
General + colorectal cancer	82.34 ± 12.17	82.6 ± 10.08	− 0.26 (− 1.81, 1.29)	0.741

Table 3 Effect of case-control status on standardized FACT scores

Covariate	FACT–Colorectal Cancer				FACT–General + Colorectal Cancer			
	Coefficient	SE	OR (95% CI)	*p* value	Coefficient	SE	OR (95% CI)	*p* value
Case status								
Case	− 2.75	0.88	0.06 (0.01, 0.36)	0.002*	1.28	0.86	3.60 (0.67, 19.41)	0.137
Control	Ref	-	-	-	Ref	-	-	-
Age (continuous, centered at 60 years)	0.71	0.44	2.03 (0.86, 4.82)	0.104	1.01	0.43	2.75 (1.18, 6.38)	0.019*
Sex								
Male	3.25	0.89	25.79 (4.51, 145.58)	< 0.001*	1.61	0.87	5 (0.91, 27.53)	0.066
Female	Ref	-	-	-	Ref	-	-	-
Race								
White	Ref	-	-	-	Ref	-	-	-
Other	1.39	0.99*	4.01 (0.58, 27.95)	0.163	0.37	0.98	1.45 (0.21, 9.88)	0.704
Relationship status								
Partner	0.84	1.06	2.32 (0.29, 18.50)	0.427	1.59	1.04	4.90 (0.64, 37.65)	0.127
Single	Ref	-	-	-	Ref	-	-	-
Education								
≤ High school	Ref	-			Ref	-	-	-
Some college	1.66	1.31	5.26 (0.40, 68.55)	0.202	0.81	1.28	2.25 (0.18, 27.63)	0.529
≥ College	2.22	1.21	9.21 (0.86, 98.65)	0.065	3.14	1.18	23.10 (2.29, 233.41)	0.008*
Insurance								
None	− 4.26	2.26	0.01 (0.0002, 1.18)	0.060	− 1.09	2.22	0.34 (0.004, 26.081)	0.623
Public	− 2.15	1.13	0.12 (0.01, 1.07)	0.056	− 2.90	1.11	0.06 (0.006, 0.485)	0.009*
Private	Ref	-	-	-	Ref	-	-	-
Charlson Comorbidity Index								
0	Ref	-	-	-	Ref	-	-	-
1	− 3.40	1.17	0.0334 (0.0034, 0.3306)	0.004*	− 5.30	1.15	0.0050 (0.001, 0.048)	< 0.001*
≥ 2	− 8.18	1.25	0.0003 (0.00003, 0.0027)	< 0.001*	− 8.39	1.23	0.0002 (0.00002, 0.002)	< 0.001*

found that overall QoL improved over time; however, measures of psychological distress remained stable [13]. According to a German population-based study evaluating a cohort of 439 individuals with CRC at 1, 3, 5, and 10 years after diagnosis, QoL measures relating to fatigue, pain, physical, and cognitive function, and global QoL declined significantly between 3 and 10 years post-diagnosis [18]. Quality of life measures relating to nausea, vomiting, and constipation remained stable [18]. Of note, this study included comparisons with historical control data and had a relatively small sample size of full responders ($n = 117$) [18].

Our findings are consistent with contemporary reports that suggest that overall QoL in CRC survivors approaches population baseline levels of QoL over time [15, 20, 26–28]. A study published by Hart et al. in 2018 compared 296 long-term CRC survivors (≥ 15 years from diagnosis) and 255 sex-matched controls recruited from the Ontario Familiar Colorectal Cancer Registry and determined that QoL was comparable or better among survivors, with the exception of bowel-related symptoms [20]. Another large investigation published in 2016 compared survey data from approximately 1000 long-term CRC survivors (≥ 5 years from diagnosis) identified via the Seattle Colorectal Cancer Registry against the American general population and concluded that most individuals who survive at least 5 years from CRC diagnosis can expect to experience age-typical QoL [15]. However, Adams et al. noted that factors such as smoking, obesity, lower levels of education, and presence of comorbidities were associated with lower physical QoL, which in turn was associated with higher risk of mortality [15].

It has been shown that comorbidities have a significant negative impact on QoL among cancer survivors, regardless of cancer type [21]. A study of female long-term CRC survivors concluded that health-related QoL was similar among survivors and women in the general population; aging and chronic medical conditions exerted a greater negative impact on QoL than the initial cancer diagnosis [29]. Our findings add to the growing body of evidence that suggests that the presence of

comorbidities is more influential on overall QoL in long-term survivors than a remote cancer diagnosis [15, 19, 21].

Given the notable improvements in CRC screening and treatment over the past few decades, the population of long-term CRC survivors has grown and will continue to grow significantly—there are currently approximately one million CRC survivors in the USA [1, 4]. The ability to assure individuals suffering from the immediate physical and psychological effects of a recent CRC diagnosis that long-term survivors generally report overall QoL comparable to the general population is valuable. Survivors should be advised that digestive symptoms may persist for a decade or more post-diagnosis. This study has the potential to help establish baseline QoL outcomes in long-term CRC survivors, which in turn may be used to guide development of novel therapeutic interventions and survivorship programs. Clinicians should be made aware that the presence of comorbidities has a greater impact on QoL than cancer diagnosis in long-term CRC survivors, and general health maintenance should be emphasized. Further prospective, longitudinal research is needed to better delineate the trajectory of QoL in CRC survivors over time.

Limitations

Our study has several strengths including the size of our cohort; the inclusion of eight geographically diverse sites of data collection; the use of age- and sex-matched control subjects; analyses adjusted for age, race, education, relationship status, and comorbidities; high survey completion rates for both survivors and controls; and the use of validated cancer-specific assessments to measure QoL. However, we encountered limitations as well. Our cross-sectional design did not allow for a baseline analysis to determine the evolution of QoL over time. As mentioned above, there is a paucity of longitudinal data regarding QoL among CRC survivors.

Our findings are based on older data, and therapeutic interventions affecting subsequent quality of life have evolved since the patients in our study were diagnosed. The primary aim of our study focused on long-term QoL outcomes for individuals who completed treatment several years prior to survey completion; therefore, individuals with recurrent CRC and those with metastatic disease were excluded. Furthermore, existing literature indicates that individuals with metastatic CRC have the worst QoL and inclusion of these cases likely would have skewed our results.

We did not perform age-specific analyses due to having insufficient power to perform a subgroup analysis by age category. We did not collect data on income level or treatment type (surgical intervention/chemotherapy/radiation). In order to standardize case-control comparisons, our final analyses excluded FACT-C questions only applicable to CRC survivors with an ostomy. Lastly, we did not investigate the apparent positive impact of male sex on CRC-specific QoL (Table 3); further prospective research assessing potential effect modifiers is necessary to clarify this association.

Conclusion

Quality of life among long-term colorectal cancer survivors is similar to that of control subjects, with the exception of CRC-specific measures relating to digestive function. Higher comorbidity indices were independently associated with poor quality of life for both cases and controls. Survivors and their healthcare providers should be aware that long-term QoL is comparable to the general population; however, there is potential that digestive tract-specific issues may persist.

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Compliance with ethical standards

Conflict of interest The authors declare that they no conflicts of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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