

# Risk and predictors of suicide in colorectal cancer patients: a Surveillance, Epidemiology, and End Results analysis

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## ABSTRACT

**Background** The risk of suicide is higher for patients with colorectal cancer (CRC) than for the general population. Given known differences in morbidity and sites of recurrence, we sought to compare the predictors of suicide for patients with colon cancer and with rectal cancer.

**Methods** Using the U.S. Surveillance, Epidemiology, and End Results database, adult patients with confirmed adenocarcinoma of the colon or rectum during 1973–2009 were identified. Parametric and nonparametric tests were used to assess selected variables, and Cox proportional hazards regression models were used to determine predictors of suicide.

**Results** The database identified 187,996 patients with rectal cancer and 443,368 with colon cancer. Compared with the rectal cancer group, the colon cancer group was older (median age: 70 years vs. 67 years;  $p < 0.001$ ) and included more women (51% vs. 43%,  $p < 0.001$ ). Suicide rates were similar in the colon and rectal cancer groups [611 (0.14%) vs. 337 (0.18%),  $p < 0.001$ ]. On univariate analysis, rectal cancer was a predictor of suicide [hazard ratio (HR): 1.26; 95% confidence interval (CI): 1.10 to 1.43]. However, after adjusting for clinical and pathology factors, rectal cancer was not a predictor of suicide (HR: 1.05; 95% CI: 0.83 to 1.33). In the colon cancer cohort, independent predictors of suicide included older age, male sex, white race, and lack of primary resection. The aforementioned predictors, plus metastatic disease, similarly predicted suicide in the rectal cancer cohort.

**Conclusions** The suicide risk in CRC patients is low (<0.2%), and no difference was found based on location of the primary tumour. Sex, age, race, distant spread of disease, and intact primary tumour were the main predictors of suicide among CRC patients. Further studies and interventions are needed to target these high-risk groups.

**Key Words** Colorectal cancer, suicide, predictors, population-based studies, SEER database

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## INTRODUCTION

Cancer is a devastating illness both physically and mentally<sup>1,2</sup>. A diagnosis of cancer has been associated with an increased risk of suicidal ideation or attempts<sup>3–6</sup>, and suicide is one of the leading causes of non-cancer-related mortality<sup>7</sup>. In recent years, significant advances in the treatment of cancer have led to increased awareness about survivorship issues and the significant psychosocial burden experienced by cancer patients<sup>1–3,6</sup>.

Several studies, mostly from Europe, have demonstrated an increased incidence of suicide among cancer patients<sup>8–17</sup>. In one large U.S. study, Misono *et al.*<sup>17</sup> demonstrated that the incidence of suicide was nearly doubled in cancer patients compared with the general population, with variation by the anatomic cancer site. Higher suicide rates were associated with male sex, white race, unmarried status, and advanced disease at the time of diagnosis<sup>17</sup>.

Colorectal cancer (CRC) is the 3rd most common cancer and the 3rd leading cause of cancer mortality in

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the United States. The lifetime risk of CRC is estimated to be 1 in 20<sup>18,19</sup>. Although previous studies have demonstrated an increased risk of suicide in CRC patients<sup>9,15,17</sup>, the predictors of suicide in that population have yet to be determined. In addition, despite CRC being commonly discussed as a single entity, morbidity is increased for rectal cancer compared with colon cancer because of greater ostomy rates and local complications from recurrent or advanced disease in the pelvis. In rectal cancer, about 75% of patients will have a defunctioning stoma or end colostomy, which, compared with primary anastomosis, carries a higher risk of postoperative complications, prolonged hospital stay, and increased mortality<sup>20</sup>. Consequently, the objective of our study was to examine the incidence and predictors of suicide for patients with rectal cancer and with colon cancer.

## METHODS

The Surveillance, Epidemiology, and End Results (SEER) program (<http://seer.cancer.gov>) of the U.S. National Cancer Institute is a conglomerate of 18 cancer registries in the United States. The program collects data about cancer incidence and mortality; it is the only comprehensive source of population-based information in the United States that includes stage of cancer at the time of diagnosis and patient survival data. The demographic distribution, incidence, and survival data relating to cancer in the SEER database registries is considered representative of the entire U.S. population<sup>21</sup>. To access the SEER data, we signed and submitted a SEER Research Data Agreement form through the SEER Web site. Upon acceptance, access to the data and the SEER\*Stat software was granted.

### Study Population and Covariates

Using SEER data from 1973–2009, we identified adult patients with a confirmed pathology diagnosis of adenocarcinoma of the colon or rectum [*International Classification of Diseases for Oncology*, 3rd edition, codes C18.0–C18.9 (colon cancer) and C19.9–C20.9 (rectal cancer)]. The outcome of interest was a cause of death designated as Suicide and Self-inflicted Injury (code 50220). Adjustments were made for demographic and disease covariates—specifically, age at diagnosis, sex, race (white, African American, or other), marital status (single, married, or unknown status), primary tumour site (colon vs. rectum), stage at diagnosis (local or regional vs. distant), number of primary tumours, and whether surgery to the primary site was performed. Our assessed outcomes were mortality rates as well as suicide rates for the colon and rectal cancer cohorts.

### Statistical Analysis

We used parametric and nonparametric statistical tests to assess cohort characteristics. We applied the chi-square test for comparisons of categorical variables according to cancer type. For continuous variables, either the Student t-test or the Wilcoxon rank-sum test was used. All comparisons were two-tailed, with  $p < 0.05$  indicating significance. To assess predictors of suicide between and within the cancer cohorts, we used Kaplan–Meier survival analysis and multivariate adjusted Cox proportional hazards regression

models. We used the SAS software application (version 9.4; SAS Institute, Cary, NC, U.S.A.) for our analysis.

## RESULTS

### Characteristics of the Study Population

In the SEER database, 631,364 adults with a confirmed diagnosis of colorectal adenocarcinoma were identified, of whom 443,368 (70.2%) had colon cancer and 187,996 (29.8%) had rectal cancer.

Patients with colon cancer were slightly older than those with rectal cancer (median age: 70 years vs. 67 years,  $p < 0.0001$ ). Colon cancer was equally distributed between men and women. In contrast, rectal cancer was more common in men than in women [106,408 (57%) vs. 81,588 (43%),  $p < 0.0001$ ]. However, despite the observations of statistical significance, differences between the cohorts were not meaningful. For instance, most patients were married, of white race, had locoregional disease, and underwent surgical resection of the primary tumour. Table 1 shows further details about the baseline characteristics of the cohorts.

Median survival was modestly longer in patients with rectal cancer than in those with colon cancer (38 months vs. 35 months,  $p < 0.0001$ ). At the time of the present analysis, 112,535 (60%) rectal cancer patients and 279,066 (63%) colon cancer patients had died. Suicide as the primary cause of death was documented in only 337 rectal cancer patients (0.18%) and 611 colon cancer patients (0.14%), representing 0.30% and 0.22% of all deaths respectively.

### Predictors of Suicide in the CRC Cohort

The risk of suicide was highest in men [hazard ratio (HR): 7.56; 95% confidence interval (CI): 5.34 to 10.70]. Other available patient demographics that predicted a higher risk of suicide included older age (>70 years HR: 1.55; 95% CI: 1.23 to 1.94), white race (HR: 3.21; 95% CI: 1.75 to 5.88), and a marital status of single (HR: 1.56; 95% CI: 1.14 to 2.13). In contrast, associations between disease-related characteristics and the risk of suicide were inconsistent. For example, metastatic disease (M1) at diagnosis (HR: 1.58; 95% CI: 1.13 to 2.21) and lack of primary tumour resection—that is, primary tumour *in situ* (HR: 2.83; 95% CI: 1.97 to 4.05)—were associated with a higher risk of suicide. Conversely, no clear correlation of suicide with other features of the primary tumour such as location [rectum vs. colon (HR: 1.05; 95% CI: 0.83 to 1.33)] or presence of multiple primary tumours (HR: 1.05; 95% CI: 0.82 to 1.35) was observed. Table 2 shows further details about the associations of patient and disease characteristics with the risk of suicide.

### Predictors of Suicide in the Rectal and Colon Cancer Cohorts

As in the CRC cohort, male sex was highly predictive of suicide in the rectal and colon cancer cohorts alike (rectal cancer HR: 9.91; 95% CI: 4.83 to 20.36; colon cancer HR: 6.82; 95% CI: 4.58 to 10.16). Additionally, suicide was more highly associated with older age (>70 years) and white race. In contrast, marital status was not a predictor of suicide in the two sub-cohorts. Interestingly, having metastatic disease at diagnosis (M1) was associated with a higher risk of suicide in the rectal cancer cohort (HR: 1.92; 95% CI: 1.12

**TABLE I** Baseline characteristics of the colorectal cancer cohort

Characteristic	Tumour site		p Value
	Rectum	Colon	
Patients (n)	187,996	443,368	
Median age (years)	67	70	<0.0001
Sex [n (%)]			
Men	106,408 (57)	218,130 (49)	<0.0001
Women	81,588 (43)	225,238 (51)	
Marital status [n (%)]			
Single	19,927 (11)	43,889 (10)	<0.0001
Married	159,601 (85)	382,033 (86)	
Unknown	8,468 (5)	17,446 (4)	
Race [n (%)]			
White	156,363 (83)	368,269 (83)	<0.0001
African American	15,328 (8)	45,112 (10)	
Others	16,305 (9)	29,987 (7)	
Primary site surgery [n (%)]			
Yes	87,259 (46)	228,129 (51)	<0.0001
No	19,574 (11)	25,426 (6)	
Unknown	81,163 (43)	189,813 (43)	
Stage [n (%)]			
Locoregional (M0)	147,754 (79)	343,608 (77)	<0.0001
Metastatic (M1)	28,067 (15)	83,929 (19)	
Unknown	12,175 (6)	15,831 (4)	
Survival (months)			
Median	38	35	<0.0001
Interquartile range	14–88	11–86	
Deaths [n (%)]	112,535 (60)	279,066 (63)	<0.0001
Suicides [n (%)]	337 (0.18)	611 (0.14)	<0.0001

to 3.30), but not in the colon cancer cohort. Table II shows further details about the predictors of suicide in the rectal and colon cancer cohorts.

## DISCUSSION

An increased incidence of suicide in cancer patients compared with the general public has been demonstrated by several studies<sup>8–12,14,15,17</sup>. Specific tumour sites associated with the highest risk of suicide include lung<sup>22</sup>, stomach<sup>17</sup> and oral cavity<sup>23</sup>. In prior studies, the risk of suicide was found to be higher in CRC patients than in the general population (29.1 per 100,000 person-years; standardized mortality ratio: 1.9; 95% CI: 1.74 to 2.07)<sup>17</sup>; however, to our knowledge, no prior study has assessed the predictors of suicide in CRC patients specifically. As was found for other tumour sites<sup>13,17,22,23</sup>, we confirm the associations of several patient-related risk factors (such as male sex, white race, and advanced age) with suicide in CRC patients. Those characteristics are similarly predictive of suicide in the general population<sup>24</sup>.

Advanced stage at time of diagnosis was also associated with the risk of suicide in CRC patients in our study.

That observation is likely multifactorial and not merely a reflection of the poor prognosis associated with advanced stage, which has previously been shown to increase the likelihood of suicide<sup>10,15,17,25</sup>. The desire for hastened death in advanced and terminally ill cancer patients correlates with physical symptoms, quality of life, and the perception of being a burden to others<sup>6</sup>. In addition, an increase in morbidity, declining performance status, and the need for ongoing treatment (all commonly seen in advanced cancer patients) increase the risk for comorbid depression<sup>1</sup> and apply significant stress, both perceived and actual, on caregivers<sup>26–29</sup>. Patients could view suicide as a strategy to relieve stress on the family.

Another significant predictor of suicide in our study was a lack of surgical resection of the primary tumour in both the colon and the rectal cohorts. An intact primary site might lead to more local symptoms such as pain, further contributing to the psychological burden of the disease. Retrospective studies have suggested a possible improvement in mortality if the primary tumour is resected in the setting of advanced disease<sup>30,31</sup>, and prospective studies are underway to evaluate the effect of resection on overall survival, progression-free survival, and quality of life<sup>32</sup>. Whether performing resections in patients with advanced CRC will translate into a decreased risk of suicide has yet to be determined.

We hypothesized that because of the differences in recurrence patterns and therapies (and therapy side effects) in rectal and colon cancer, differences in suicide rates might be evident. Rectal cancer is associated with significant morbidity related to the increased rates of stoma and to the devastating consequences of locally advanced and recurrent disease, such as significant pain and spinal cord compression. On univariate analysis, a rectal-site cancer was a predictor of suicide; however, when controlling for other important covariates, a multivariate analysis failed to identify the site of the primary tumour as a predictor of suicide. A potential explanation for that finding could be related to the timing of suicide. The risk of suicide is felt to be strongest very early after diagnosis<sup>14–16,33</sup>. Fang *et al.*<sup>15</sup> found that the highest risk fell within the first 12 weeks after diagnosis (relative risk: 4.7) and that the risk lessened after that time (relative risk at 12–52 weeks: 2.1; relative risk at 52 weeks and beyond: 1.6). Those observations suggest that suicide in cancer patients is possibly more related to the initial psychological burden of diagnosis than to the accumulating morbidity from the disease or the side effects of treatment.

Despite a declining risk of suicide over time, the risk level remains elevated even decades after diagnosis, suggesting a long-lasting effect on quality of life for survivors<sup>1,34</sup>. Although our study showed stronger associations of suicide with non-modifiable factors (sex, age, race, and marital status), special attention to this high-risk patient population and, possibly, interventions to support their psychological well-being might help to reduce the risk of suicide. Such attention is particularly important for cancers with a potentially higher cure rate, such as CRC.

Inherent to its design, our study has limitations. Potential confounders such as coexisting medical and psychiatric conditions and substance abuse could not

**TABLE II** Adjusted multivariate analysis of predictors of suicide in the colorectal cancer (CRC) cohort

Characteristic	Tumour site					
	All CRC		Rectum		Colon	
	HR	95% CI	HR	95% CI	HR	95% CI
Age group						
<70 Years	Reference		Reference		Reference	
≥70 Years	1.55	1.23 to 1.94	1.54	1.06 to 2.23	1.49	1.13 to 1.96
Sex						
Women	Reference					
Men	7.56	5.34 to 10.70	9.91	4.83 to 20.36	6.82	4.58 to 10.16
Marital status						
Married	Reference		Reference		Reference	
Single	1.56	1.14 to 2.13	NS		NS	
Unknown	1.05	0.61 to 1.80				
Race						
African American	Reference		Reference		Reference	
White	3.21	1.75 to 5.88	3.40	1.08 to 10.75	3.03	1.49 to 6.17
Others	2.02	0.96 to 4.26	1.64	0.41 to 6.56	2.23	0.92 to 5.38
Stage						
Locoregional (M0)	Reference		Reference		Reference	
Metastatic (M1)	1.58	1.13 to 2.21	1.92	1.12 to 3.30		NS
One primary tumour						
No	Reference		NS		NS	
Yes	1.05	0.82 to 1.35				
Site of primary						
Colon	Reference		—		—	
Rectum	1.05	0.83 to 1.33				
Primary site surgery						
Yes	Reference		Reference		Reference	
No	2.83	1.97 to 4.05	2.82	1.71 to 4.66	2.82	1.66 to 4.80

HR = hazard ratio; CI = confidence interval; NS = nonsignificant.

be evaluated because that information is not collected by the SEER program. In addition, details of therapeutic interventions for cancer are not adequately captured in the SEER database and could have affected the results. Finally, misclassifications of the cause of death (specifically, suicide) could have led to an underrepresentation of that outcome in our analysis.

## CONCLUSIONS

The risk of suicide in CRC patients did not vary based on the location of the primary tumour, but our study did identify a number of risk factors for suicide in both colon and rectal cancer patients. The information presented here might help to identify patients at higher risk of suicide, for whom screening and early interventions might improve psychological well-being.

## CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology's* policy on disclosing conflicts of interest, and we declare that we have none.

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