Cardiovascular-Specific Mortality and Risk Factors in Colorectal Cancer Patients: A Cohort Study Based on Registry Data of Over 500,000 Individuals in the US

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Abstract:

Background: Colorectal cancer (CRC) is one of the most common cancers worldwide, and recent studies have found that CRC patients are at increased risk for cardiovascular disease (CVD). This study aimed to investigate competing causes of death and prognostic factors among a large cohort of CRC patients and to describe cardiovascular-specific mortality in relation to the US standard population.

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Methods: This registry-based cohort study identified patients diagnosed with CRC between 1973 and 2015 from the Surveillance, Epidemiology, and End Results (SEER) database in the US. Cumulative mortality functions, conditional standardized mortality ratios, and cause-specific hazard ratios were calculated.
Results: Of the 563,298 eligible CRC patients included in this study, 407,545 died during the follow-up period. CRC was the leading cause of death, accounting for 49.8% of all possible competing causes of death. CVD was the most common non-cancer cause of death, accounting for 17.8% of total mortality. This study found that CRC patients have a significantly increased risk of cardiovascular-specific mortality compared to the US standard population, with the risk increasing with age and extended survival time.
Conclusion: This study highlights the need to develop multidisciplinary prevention and management strategies for CRC and CVD to improve CRC patients' survival and quality of life.

Keywords: Colorectal cancer; Cardiovascular diseases; Non-cancer deaths; Surveillance; Epidemiology; Standardized mortality ratios

1. Introduction

Colorectal cancer (CRC) is a major global health issue, with more than 1.9 million new cases and 935,000 deaths in 2020, making it the third most frequently diagnosed malignancy and the second leading cause of cancer-related death worldwide[1]. Recent advancements in cancer prevention, diagnosis, and treatment have significantly improved CRC survival rates[2]. The 5-year relative survival rate for CRC in the United States has increased by 10% for the approximately 1.4 million colorectal cancer patients currently being treated[3]. While CRC-related deaths have plateaued, researchers are now seeking to identify other factors that increase the risk of death to improve the survivorship of CRC.

Recent studies have found that patients with CRC are 2-4 times more likely to develop cardiovascular disease (CVD) than individuals without CRC[4]. For instance, older CRC patients are at a higher risk of developing new-onset morbidities related to CVD, with a 10-year cumulative incidence rate of 57.4% compared to 22% for controls[5]. The shared multiple risk factors of both diseases may explain the increased risk of CVD among CRC patients. Non-modifiable factors such as genetic factors, race, sex, age, and family history have been shown to be associated with the incidence of both CVD and CRC[6,7]. A variety of modifiable behavioral and lifestyle factors, such as smoking, alcohol consumption, unhealthy diet, physical inactivity, and obesity, were all reported to increase the risk of both CVD and CRC[7-11]. One possible mechanism linking CRC to increased CVD risk may be the gut microbiota dysbiosis involved in CRC pathogenesis[12,13], which has been shown to increase the occurrence of atherosclerosis and CVD[14,15].

Despite the known epidemiological link and common risk factors between CRC and CVD, studies investigating the incidence of CVD-related deaths among CRC patients remain lacking. Though a range of factors have been identified to affect both CRC and CVD, no study has specifically investigated the independent risk factors of CVD-related mortality among CRC patients. To fill the research gap, we followed up with a nationally representative cohort of CRC patients in the US to investigate their long-term CVD-specific mortality relative to the US standard population. Based on previous literature reviews, a list of potential risk factors of CVD among CRC patients was selected. Previous studies have consistently reported higher rates of CRC and CVD in

men than women[16-18], indicating sex is a significant risk factor for CVD among CRC patients. In addition, previous studies also showed that the risk of CVD and related death increased with increasing age and diagnosis time[2,5,19], we would expect age and diagnosis time may be related to CVD risk among CRC patients. Furthermore, cancer-related treatments, such as surgery, chemotherapy, and radiotherapy, have been shown to contribute to the increased incidence of CVD deaths among patients with cancer[20,21], we thus expected that cancer-related treatments might also affect the occurrence of CVD among CRC patients. We also included the characteristics of tumors, such as tumor number, location, and stage, as potential risk factors for CVD, though these factors were less studied and reported.

2. Methods and Materials

2.1. Data Sources

All data were retrieved from the Surveillance, Epidemiology, and End Results (SEER) database (https://seer.cancer.gov/), which is a clinical database funded by the National Cancer Institute (NCI) to collect cancer incidence, prevalence, and survival data from US cancer registries covering approximately 30% of the US population[22]. For this registry-based retrospective cohort study, demographic characteristics, clinical characteristics, treatment, and survival data on CRC patients were retrieved from the SEER database. Demographic characteristics included age, sex, and race. Clinical characteristics included the year of tumor diagnosis, as well as grading, stage, site, and number of tumors. Treatment data included surgery, chemotherapy, and radiotherapy, while survival data included the number of deaths, crude death rates, age-adjusted death rates, and causes of death.

To compare with the general population, cardiovascular-specific mortality of the general US population between January 1, 1973, and December 31, 2015, was selected from the underlying cause of death (WONDER) online database by the Centers for Disease Control and Prevention (CDC). WONDER is a national database providing county-level national mortality and population data spanning 1999-2020. For this registry-based retrospective cohort study, both demographic and mortality data were extracted from the WONDER databases. Demographical data included age, sex, race, year, and place of residence. Mortality data included the number of deaths, crude death rates, age-adjusted death rates, and causes of death. Our study is based on a publicly available anonymized database, and thus exempt from ethical compliance.

2.2. Study Population

All patients with a first primary malignant CRC diagnosis (ICD: C18-20) between January 01, 1973, and December 31, 2015, were extracted from the SEER 18 database[23,24]. Patients with duplicate data (3.11%), unknown surgery information (0.27%), unknown stage (2.32%), unknown clinical outcome (1.54%), unknown survival data (0.07%), unknown grade (21.17%), or unknown tumor location (0.46%) were excluded to perform a complete case analysis. The screening process is shown in Figure 1.

This study focused on CVD diseases, identified using ICD-10 codes I00-I99. The CVD diseases included acute rheumatic fever (I00-I02), chronic rheumatic heart diseases (I05-I09), hypertensive heart disease (I11), hypertensive heart and renal disease (I13), ischemic heart diseases(I20-I25), pulmonary heart disease and diseases of pulmonary circulation(I26-I28), as well as other forms of heart disease (I30-I51).

2.3. Statistical Analysis

The continuous and categorical variables distributions were expressed as means ± standard

deviations and frequencies (percentages), respectively. Group differences were analyzed by Student's t-test for continuous variables and by chi-square or Wilcoxon rank sum test for categorical variables. We calculated and plotted overall crude cumulative mortality functions for specific deaths due to CVD, CRC, other cancers, and other noncancerous diseases stratified by demographical and clinical factors and analyzed the variability of cumulative mortality between subgroups by Gary's test. In addition, adjusted cause-specific hazard ratios (HRs) were calculated to estimate the relative associations of individual risk and prognostic factors for cardiac and colorectal cancer-related deaths. To explore the latent correlation between the variables, we used Spearman's correlation test and determined the strength of the association based on the absolute value of Spearman's correlation coefficient[25]. All analyses were conducted using R version 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria). A two-sided test with $P<0.05$ indicates statistical significance[26].

3. Results

3.1. Patient Characteristics

A total of 792,937 CRC cases were identified between 1973 and 2015, out of which 563,298 (71.03%) met the inclusion criteria and were included in this study (Figure 1). The median follow-up time for the patients was 6.67 ± 6.48 years. Most patients were over 50 (91.5%) and white (83.3%), and half were male (50.9%). There were significant differences in the distribution of CRC patients between the treated (radiotherapy, chemotherapy, or surgery) and untreated groups, with 11.6% vs. 88.4%, 29.1% vs. 70.9 %, and 94.1% vs. 5.9%, respectively. CRC was most common in the sigmoid colon (21.9%). Over the follow-up period, 36.0% of patients died from CRC, 12.9% died from cardiovascular disease, and the 5-year and 10-year survival rates of the CRC patients were 51.37% and 35.84%, respectively. The baseline characteristics of the included CRC patients are summarized in Supplemental Table 1.

3.2. Cumulative Mortality

The cumulative mortalities for all causes of death among CRC patients are illustrated in Figure 2. The results demonstrated that CRC had the highest cumulative mortality, followed by other non-cancer causes of death that were unrelated to CVD. Cardiovascular-specific cumulative mortality was significantly higher than cumulative mortality due to cancers other than CRC.

When stratified by age groups, patients younger than 50 had the highest cumulative CRC mortality compared with cardiovascular-specific deaths. Nevertheless, it was observed that the cumulative cardiovascular-specific mortality steadily increased with age at diagnosis and length of follow-up (Figure 3). Similar methods were used for stratification by other indicators, and the results are shown in supplementary Figures 1-7. When stratified by sex, no significant difference was observed in cumulative CRC or cardiovascular-specific mortality (Supplementary Figure 1). When stratified by the year of diagnosis, patients diagnosed during 1973-2000 had the highest cumulative cardiovascular-specific mortality with the longest follow-up (Supplementary Figure 2).

Moreover, stratification by treatment revealed that patients who underwent chemotherapy or radiation had a lower cumulative cardiovascular mortality than patients with no or unknown treatment (Supplementary Figure 3). Furthermore, when stratified by the number of primary tumors or surgery, it was found that only one primary tumor patient or the surgical patient had a relatively higher cumulative cardiovascular mortality (Supplementary Figure 4). Stratification by tumor grade showed that cumulative cardiovascular mortality decreased with increasing tumor grade (Supplementary Figure 5). Additionally, when stratified by the clinical stage of the tumor,

cumulative cardiovascular mortality was highest in patients with local tumors at the first diagnosis, surpassing cumulative mortality from CRC approximately 12 years after diagnosis, while it was lowest in patients with remote metastatic tumors at the first diagnosis (Supplementary Figure 6). Lastly, when stratified by tumor site, the cumulative cardiovascular mortality was approximately 0.2 at the corresponding anatomical sites where colon cancer may occur, although the cumulative cardiovascular mortality was slightly higher in patients with CRC at the cecum, appendix, and ascending colon (Supplementary Figure 7).

3.3. Conditional Standardized Mortality Ratios (cSMR)

The comparison of cardiovascular-specific mortality between CRC patients and the general population is shown in Supplemental Table 2. The analysis of age-standardized cardiovascular-specific mortality revealed that cSMRs were significantly increased for all age groups. In terms of all-cause mortality, CRC patients showed an over 371-fold increase in mortality among younger individuals, with a cSMR of 371.66 (95% CI: 366.75-376.62) for those under 50 years of age. This elevated mortality risk steadily decreased with increased age.

3.4. Cause-specific Hazard Ratios (HRs)

The association between individual prognostic factors and cardiovascular-specific mortality among CRC patients is presented in Table 1. As shown, age was the most influential factor on cardiovascular-specific mortality, with patients aged 50-64, 65-74, and ≥75 having hazard ratios (HRs) of 3.395 (95% CI 3.152-3.656), 6.865 (95% CI 6.383-7.383), and 11.993 (95% CI 11.152-12.898), respectively, compared to patients aged <50. Additionally, patients who received cancer-direct surgery had a 19% decreased risk of cardiovascular-specific mortality [HRs 0.810 (95% CI 0.772-0.850)] relative to those without surgery. Furthermore, patients who received radiotherapy or chemotherapy had a decreased risk of cardiovascular-specific mortality compared to those who did not receive either treatment, with HRs of 0.902 (95% CI 0.871-0.933) and 0.624 (95% CI 0.609-0.640), respectively. Patients diagnosed with CRC between 2001-2005 and 2006-2015 had a 33.6% and 50.8% decreased risk of cardiovascular-specific mortality, respectively, relative to those diagnosed before 2000, with HRs of 0.664 (95% CI 0.652-0.676) and 0.492 (95% CI 0.481-0.504). Patients diagnosed with multiple primary tumors had a 28.8% decreased risk of cardiovascular-specific mortality [HRs 0.712 (95% CI 0.700-0.724)] compared to those diagnosed with only one primary tumor. The difference in cardiovascular-specific mortality was not statistically significant in patients diagnosed with local or regional tumors compared with CRC in situ but was significantly lower in patients with distal CRC [HRs 0.294 (95% CI 0.222-0.388)]. We also observed that grading was associated with a decrease in cardiovascular-specific mortality, with HRs (95% CIs) of 0.918 (0.900-0.937), 0.832 (0.811-0.855), and 0.802 (0.743-0.866) for patients with grading II, grading III, grading IV relative to grading I. Moreover, there was no significant difference in the risk of cardiovascular-specific death between patients with CRC located in the cecum, appendix, and ascending colon compared to those with CRC in the transverse colon and hepatic or splenic flexure of the colon. However, patients with CRC in transverse colon and hepatic or splenic flexure of colon and descending colon, sigmoid colon, and rectosigmoid junction were at a slightly lower risk for cardiovascular death [HRs 0.959 (95% CI 0.942-0.977) and HRs 0.919 (95% CI 0.897-0.942), respectively], whereas patients with overlapping lesion or tumors involving multiple locations were at a slightly higher risk [HRs 1.050 (95% CI 1.012-1.089)].

4. Discussion

As far as we know, this is the first and most extensive registry-based study on cardiovascular-specific mortality and risk factors among CRC patients, making the presented work unique. We conducted a study analyzing the underlying causes of death in over half a million CRC patients and found that cardiovascular-specific mortality was the most common cause of death other than CRC. This observation aligns with the well-established impact of CVD on long-term mortality. Furthermore, we observed significantly increased cSMR and all-cause mortality rates in CRC patients of all age groups by analyzing age-specific and overall standardized mortality rates in colorectal cancer relative to the standard US population from 1999-2015. This finding is consistent with a previous study, which reported that CRC patients of all ages displayed SMRs of CVD and all-cause death that were higher than those of the general population[2]. It is widely known that pathogenic CRC and CVD share many risk factors, including obesity, diabetes, chronic inflammation, alcohol, and tobacco[4,5,27-32]. Additionally, intestinal microbiota dysbiosis has been implicated in the pathogenesis of both CRC and CVD[33-35]. Studies have shown that intestinal microbiota can affect immune regulation, host energy metabolism, and oxidative stress, all of which are associated with the development of CVD[14,15]. Some investigators proposed that impaired intestinal barrier function was involved in the development of cardiovascular disease by increasing intestinal permeability, enhancing systemic inflammation, and altering intestinal immune function[36,37]. Therefore, it is reasonable to suspect that dysbiosis of the intestinal flora may mediate the link between CRC and CVD. However, further research is necessary to determine the exact mechanisms.

This study evaluated the cause-specific hazard for cardiovascular-related mortality among CRC patients as a function of demographical factors and clinical factors. We found that the hazard of CVD-caused death increased with increasing age among CRC patients, which was consistent with previous studies indicating that age was a major risk factor associated with CVD[19,38]. Our results are in line with previous research, which revealed that CVD was the primary non-cancer cause of death in elderly CRC patients[5]. This condition may be due to decreased cardiac function in elderly patients and the presence of underlying diseases such as diabetes, dyslipidemia, and hypertension. In addition, we found a strikingly high risk of cardiovascular-specific mortality among CRC patients aged under 50, who were 371 times more likely to die from CVD than the general population aged under 50. This may be explained by the relatively low cardiovascular-specific mortality in the general population who were aged under 50, as CVD mainly occurs in the elderly. Since the calculation of cSMR among CRC patients was based on the general population as the denominator, it is unsurprising that the cSMR of the under-50 age group was high when the denominator was low. This result suggests that special attention should be paid to younger CRC patients who are at high risk of cardiovascular-specific mortality, with appropriate preventive measures taken to prevent the occurrence of CVD.

Another study analyzed non-cancer causes in a sample of 834,510 CRC patients diagnosed between 1975 and 2016[2] and found that deaths from non-cancer causes increased with the time from the point of cancer diagnosis, with cardiovascular diseases being the most common non-cancer cause of death across all periods. Our work corroborates these findings, as our study demonstrated a positive association between cardiovascular-specific mortality and greater distance from the event point of CRC diagnosis. Additionally, we found that the risk of

cardiovascular-specific death decreased in CRC patients as the year of diagnosis became more recent. One explanation may be that patients diagnosed in recent years have shorter follow-ups and, therefore, were less likely to die from any cause. Another reason may be related to more advanced medical technology and better treatment plans available to those recently diagnosed patients, which improved their survival.

Our study also assessed the hazard of CVD-caused death among CRC patients as a function of surgery. We found that CRC patients undergoing surgical resection had a relatively decreased cardiovascular-specific mortality compared to those without surgery. These findings were similar to those of a retrospective cohort study that included 164,719 patients with colorectal cancer, which found that not undergoing curative surgery was an independent risk factor for cardiovascular mortality[39]. However, a recent study of a small cohort of 412 patients reported an increased risk of death due to cardiovascular disease in CRC patients who underwent surgical resection[40]. It should be noted that surgery can increase the risk of complications, including CVD, in CRC patients[41,42]. Nevertheless, nonsurgical CRC patients may also have a higher risk of cardiovascular-specific mortality due to advanced cancer progression[43,44]. The large difference in the composition of nonsurgical CRC patients and surgical CRC patients in this study may have caused statistical bias. Furthermore, different colectomy procedures are associated with varying cardiovascular disease risks[45]. Therefore, further studies are required to confirm the effect of each specific surgery on cardiovascular-specific mortality in CRC patients. We speculate that colorectal cancer surgery may reduce the incidence of CVD death by altering the gut microbes.

In further subgroup analyses, we found that patients who received radiotherapy or chemotherapy had a lower hazard of CVD-caused death compared to those without radiotherapy or chemotherapy treatment. This finding was contrary to some previous studies showing an increased risk of cardiovascular adverse events and cardiovascular-specific mortality among CRC patients who received radiotherapy or chemotherapy[19,44,46]. However, this finding was consistent with some other studies showing that radiotherapy or chemotherapy did not increase the incidence of cardiovascular adverse events among CRC patients and even resulted in a lower risk of CVD[40,47]. Although it has been widely acknowledged that radiotherapy or chemotherapy may induce cardiotoxicity in patients with CRC, such effects may be moderated or buffered by other factors, such as less aggressive cancer progression and better behavioral and lifestyle management after therapy. Another possible explanation may be related to the prior indications for radiotherapy or chemotherapy; only patients with low cardiovascular risk could receive radiotherapy or chemotherapy. Therefore, further prospective studies are required to confirm the effects of radiotherapy and chemotherapy on cardiovascular adverse events and cardiovascular-specific mortality among CRC patients.

Moreover, we were the first to evaluate the impact of the number of primary tumors on cardiovascular-specific mortality among CRC patients, finding that patients with multiple primary tumors had a lower hazard of cardiovascular-specific mortality than those with one primary tumor. Given that patients with multiple primary tumors were more likely to die from other tumors before developing CVD, it is not surprising that they had lower cardiovascular-specific mortality than patients with single primary tumors. In addition, patients with multiple primary tumors may receive more clinical attention and preventive care due to their high risk of multiple complications and mortality, which may help prevent further occurrence of CVD.

Additionally, we evaluated the cardiovascular-specific mortality among CRC patients with

disease stage or tumor grading at diagnosis, and our findings indicated that CRC patients with a diagnosis of the distant stage or with an increased grade had a significantly lower risk of cardiovascular-specific mortality compared to their respective controls (Stage at situ or grade I of CRC). This could be due to the reduction in overall survival time observed in CRC patients with the distant stage or increased tumor grade, leading to inadequate exposure to cardiovascular-specific death events. A recent study revealed a continuous increase in the number of deaths due to non-cancer causes when stratified by tumor sites among CRC patients[2]. In our study, we further clarified cause-specific HRs for cardiovascular-related mortality among CRC patients stratified by tumor sites. Compared to tumors in the cecum, appendix, and ascending colon, tumors in the transverse colon and hepatic or splenic flexure of the colon showed no significant difference in the risk of cardiovascular-specific mortality. In contrast, tumors in the descending colon, sigmoid colon, and rectosigmoid junction or in the rectum were associated with a significantly lower risk of cardiovascular-specific mortality. In comparison, overlapping lesions or tumors involving multiple locations were associated with a slightly higher risk of cardiovascular-specific mortality.

Several limitations need to be noted before interpreting the results. First, this retrospective cohort study may be subject to selection and recall bias and cannot establish causality. Second, our analysis was based on two national databases, which, though covering most of the national population, may still miss specific populations, such as undocumented residents and alien nonresidents. Third, we didn't include other potential risk factors of CVD-related mortality, such as behavioral (e.g., physical activity, sedentary time, diet) and psychological (anxiety, depression) factors, since they were not available from SEER and WONDER.

5. Conclusion

In summary, our findings emphasize the need to address CVD as a significant contributor to mortality in CRC patients. The increased risk of cardiovascular-specific mortality among CRC patients compared to the general population warrants further attention and action. It is crucial to identify and evaluate additional prognostic factors that may influence cardiovascular-specific mortality in CRC patients to develop appropriate management and prevention strategies. This study provides a basis for future research to investigate potential interventions and to develop cardio-oncological risk stratification tools for CRC patients. Improved understanding of the relationship between CRC and CVDs may help clinicians optimize patient care and improve patient outcomes.

Supplementary Materials

The following supporting information can be downloaded.

Author Contributions

All authors participated in data acquisition. T.-L.Z., H.-X.Z., H.-J.H., Y.-G.F., J.-L.Z. and M.-X.Z. contributed to the conception and design of the study. H.-H.H., W.-D.Z., L.-X.J., M.T., D.E. and W.H. performed the data analysis and interpretation. T.-L.Z., H.-X.Z., H.-J.H., Y.-G.F., J.-L.Z. and M.-X.Z. contributed to the drafting and revision of the manuscript. T.-L.Z., Y.-G.F., W.H., J.-L.Z. and M.-X.Z. contributed to funding acquisition. All authors have read and agreed to the published version of

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Informed Consent Statement

Since our research only involved analyzing patient data without using specific individual information, obtaining patient consent was waived.

Data Availability Statement

The study data were obtained by abstracting information from the Surveillance, Epidemiology, and End Results (SEER) database. The article contains all pertinent data related to the study, or it has been provided as supplementary information.

Conflicts of Interest

The authors state that they do not have any competing interests.

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Table 1. Cause-specific hazard and 95% confidence intervals for cardiovascular-related mortality among colorectal cancer patients in the US from January 01, 1973, to December 31, 2015.

Factors	Number of patients	Cause-specific hazards ratios	
		Cardiovascular	P-value
Age at diagnosis (years)			
< 50	47947	1.00 (ref.)	
50-64	150201	3.395 (3.152-3.656)	< 0.0001
65-74	158222	6.865 (6.383-7.383)	< 0.0001
≥ 75	206928	11.993 (11.152-12.898)	< 0.0001
Surgery			
No	33016	1.00 (ref.)	
Yes	530282	0.810 (0.772-0.850)	< 0.0001
Radiotherapy			
No/unknown	497946	1.00 (ref.)	
Yes	65352	0.902 (0.871-0.933)	< 0.0001
Chemotherapy			
No/unknown	399323	1.00 (ref.)	
Yes	163975	0.624 (0.609-0.640)	< 0.0001
Year of diagnosis			
≤ 2000	269323	1.00 (ref.)	
2001-2005	148725	0.664 (0.652-0.676)	< 0.0001
2006-2015	145250	0.492 (0.481-0.504)	< 0.0001
Number of primary tumors			
One	398107	1.00 (ref.)	
Multiple	165191	0.712 (0.700-0.724)	< 0.0001
Stage			
In situ	356	1.00 (ref.)	
Localized	224781	1.157 (0.879-1.524)	0.3
Regional	234669	0.920 (0.698-1.211)	0.55
Distant	103492	0.294 (0.222-0.388)	< 0.0001
Grading			
I	69849	1.00 (ref.)	
II	375542	0.918 (0.900-0.937)	< 0.0001
III	109875	0.832 (0.811-0.855)	< 0.0001
IV	8032	0.802 (0.743-0.866)	< 0.0001
Tumor site			
Cecum, appendix and ascending colon	165435	1.00 (ref.)	
Transverse colon and hepatic or splenic flexure of colon	72249	1.006 (0.982-1.029)	0.64
Descending colon, sigmoid colon and rectosigmoid junction	198842	0.959 (0.942-0.977)	< 0.0001
Rectum	99924	0.919 (0.897-0.942)	< 0.0001

Overlapping lesion or tumors involving multiple locations	26848	1.050 (1.012-1.089)	0.0093

Bold values indicate P < 0.05.

Figure 1. Flowsheet of case inclusion and exclusion criteria of CRC patients in the US from January 01, 1973, to December 31,

Figure 2. Cumulative cause-specific mortality among CRC patients in the US from January 01, 1973, to December 31, 2015.

Figure 3. Cumulative cardiovascular-specific and CRC-specific mortality by age at diagnosis among CRC patients in the US from January 01, 1973, to December 31

Highlights

- Colorectal cancer (CRC) patients have a higher risk of cardiovascular-specific death.
- Risk factors: age, tumor grade, overlapping lesion or tumors involving multiple locations.
- Protective factors: Radiotherapy, chemotherapy, surgery, multiple primary tumors, etc.
- Developing multidisciplinary prevention strategies for CRC and cardiovascular disease.

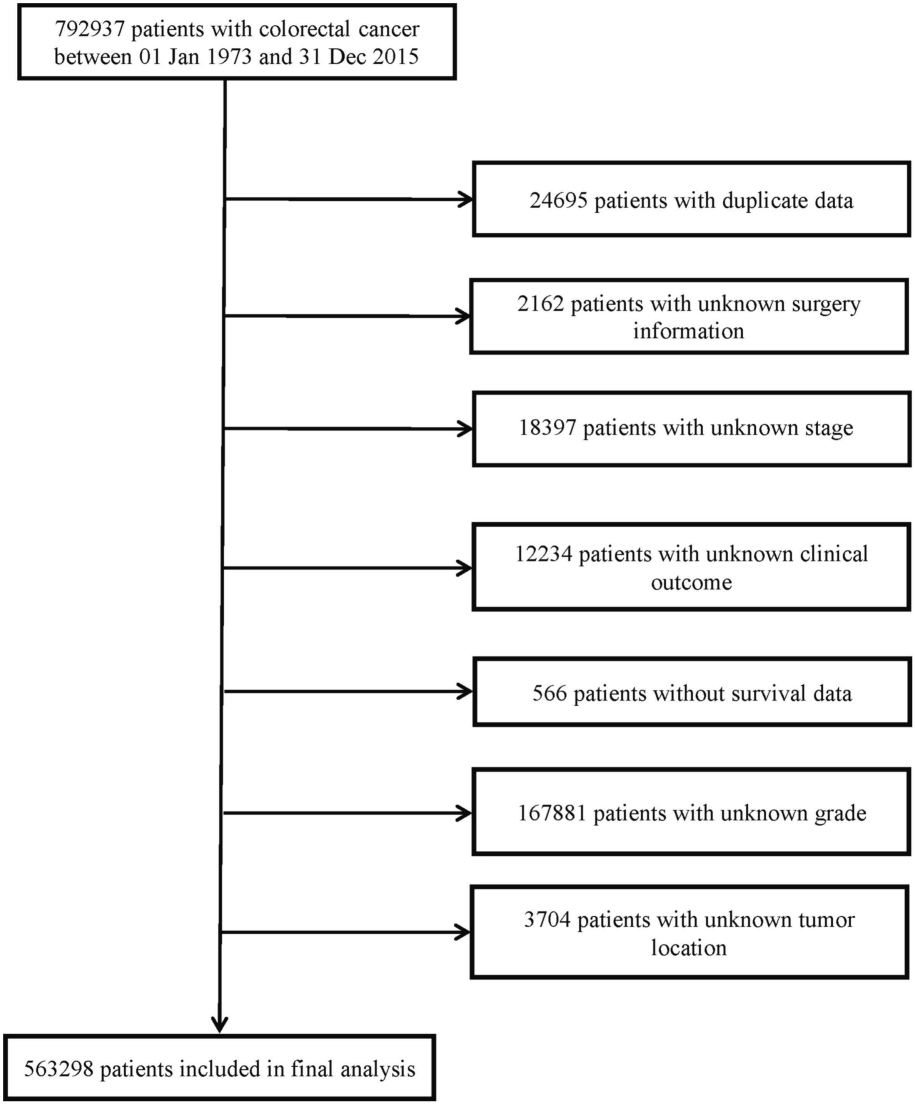
792937 patients with colorectal cancer between 01 Jan 1973 and 31 Dec 2015
24695 patients with duplicate data
2162 patients with unknown surgery information
18397 patients with unknown stage
12234 patients with unknown clinical outcome
566 patients without survival data
167881 patients with unknown grade
3704 patients with unknown tumor location
563298 patients included in final analysis

Figure 1

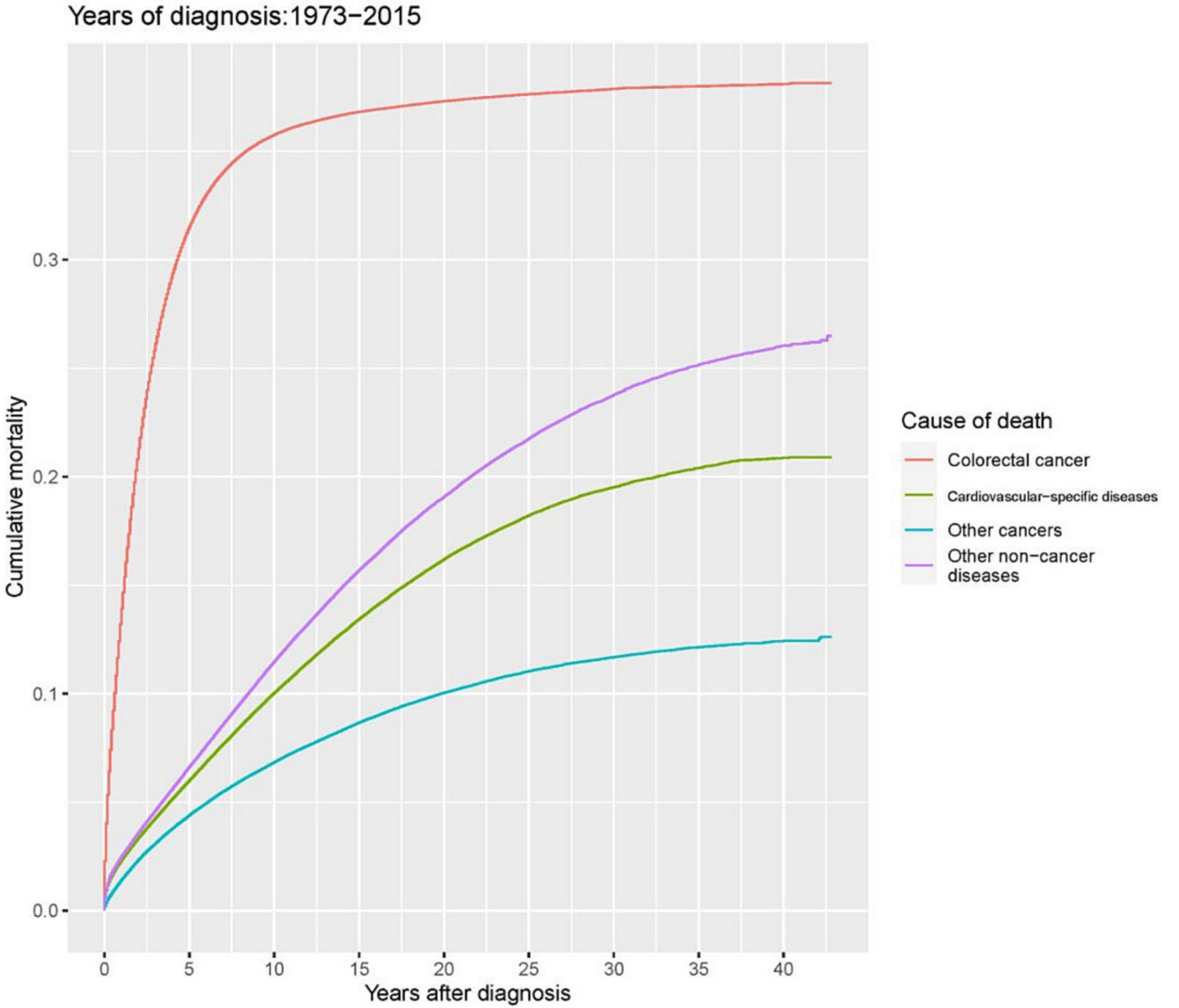
Years of diagnosis:1973−2015
Cumulative mortality
0.0
0.1
0.2
0.3
0
5
10
15
20
25
30
35
40
Years after diagnosis
Cause of death
Colorectal cancer
Cardiovascular−specific diseases
Other cancers
Other non−cancer diseases

Figure 2

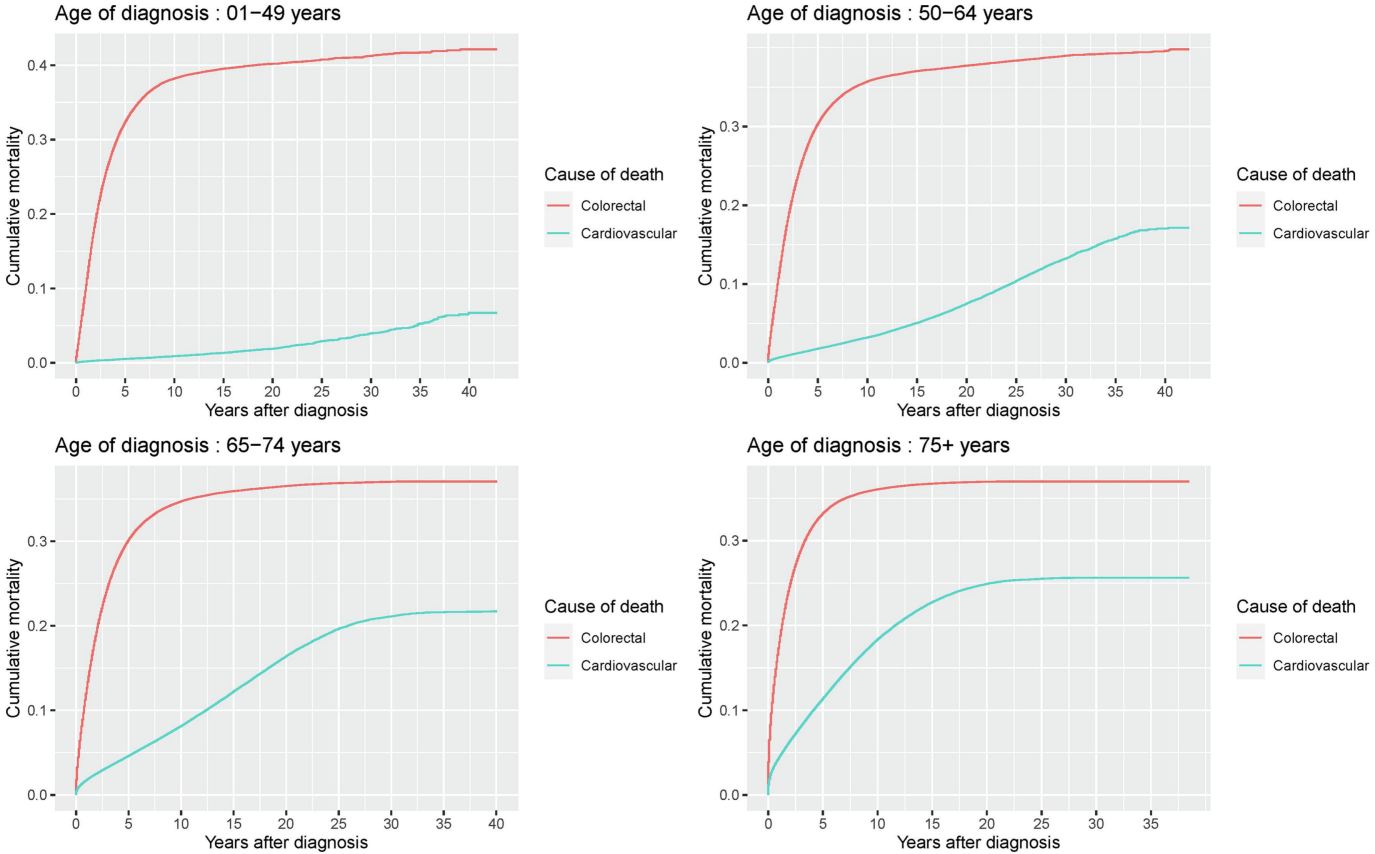
Age of diagnosis : 01−49 years
Age of diagnosis : 50−64 years
Age of diagnosis : 65−74 years
Age of diagnosis : 75+ years
Cumulative mortality
Years after diagnosis
Cause of death
Colorectal
Cardiovascular

Figure 3