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Marital status and survival in patients with rectal cancer: An analysis of the Surveillance, Epidemiology and End Results (SEER) database

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ABSTRACT

Background: Marital status has been validated as an independent prognostic factor for survival in several cancer types, but is controversial in rectal cancer (RC). The objective of this study was to investigate the impact of marital status on the survival outcomes of patients with RC.

Methods: We extracted data of 27,498 eligible patients diagnosed with RC between 2004 and 2009 from the Surveillance, Epidemiology and End Results (SEER) database. Patients were categorized into married, never married, divorced/separated and widowed groups.We used Chi-square tests to compare characteristics of patients with different marital status.Rectal cancer specific survival was compared using the Kaplan–Meier method,and multivariate Cox regression analyses was used to analyze the survival outcome risk factors in different marital status.

Results: The widowed group had the highest percentage of elderly patients and women,higher proportion of adenocarcinomas, and more stage I/II in tumor stage ($P < 0.05$),but with a lower rate of surgery compared to the married group (76.7% VS 85.4%). Compared with the married patients, the never married (HR 1.40), widowed (HR 1.61,) and divorced/separated patients (HR 1.16) had an increased overall 5-year mortality. A further analysis showed that widowed patients had an increased overall 5-year cause-specific survival(CSS) compared with married patients at stage I(HR 1.92),stage II (HR 1.65),stage III (HR 1.73),and stage IV (HR 1.38).

Conclusion: Our study showed marriage was associated with better outcomes of RC patients, but unmarried RC patients, especially widowed patients,are at greater risk of cancer specific mortality.

1. Introduction

Rectal cancer (RC) is the most common gastrointestinal cancer in males and females, and more than 39,000 people were diagnosed with rectal cancer in the United States in 2015 [1]. The incidence rate of RC had decreased over several decades through timely secondary prevention (screening),but RC is still common in the western world, and is associated with high morbidity and mortality [2]. Marital status has been proposed as an independent prognostic factor in breast, prostate, colorectal, gastric, and head/neck cancers [3–6], and unmarried patients had worse survival outcomes than married counterparts. A previous population-based analysis of the Surveillance, Epidemiology, and End Results (SEER) database showed that unmarried patients were at significantly greater risk of metastasis, undertreatment, and cancer-related death [3]. Relationship between marital status and cancer survival may reflect the health-monitoring and behavior-shaping performed by spouses [7], and married cancer patients are more likely to experience better financial support, are diagnosed at earlier stages, receive recommended treatment, and make healthier life-choices due to spousal support [8,9].

Colon and rectal cancer are usually referred to as colorectal cancer because of many similar clinicopathological features. Li Wang et al. [10] concluded that married colon cancer patients survived significantly longer than unmarried patients and Li Qingguo et al. [6] made the same conclusion about CRC patients. However, Johansen et al. [11] showed that there was no protective effect of marriage in RC patients among the Danish population. Given that RC is associated with high mortality rates in both sexes [12], the relationship between marital status and survival needs to be explored.

Our study used data from the population-based SEER database to explore the impact of marital status on survival outcomes in RC patients.

Abbreviations: CRC, colorectal cancer; RC, rectal cancer; SEER, Surveillance, Epidemiology, and End Results; ICD-O-3, International Classification of Diseases for Oncology 3rd edition; AJCC, American Joint Committee on Cancer; TNM, tumor, node, and metastasis; HR, hazard ratio; CCS, cause-specific survival; CI, confidence interval

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2. Methods

2.1. Patients

The current SEER database 1973–2013 (Version April 2016) consists of 18 tumor registries that cover approximately 26% of the population in the United States. We extracted data of 27,498 eligible patients diagnosed with primary RC between 2004 and 2009 from the SEER database (http://seer.cancer.gov). The inclusion criteria were: (1) age < 18 years at diagnosis; (2) primary sites defined by the International Classification of Diseases for Oncology 3rd Edition (ICD-O-3) codes: C20.9; (3) histologic type: adenocarcinoma (codes 8140, 8210, 8261, and 8263), mucinous adenocarcinoma (code 8480), or signet ring cell carcinoma (code 8490); (4) marital status known. Exclusion criteria were: (1) grade undefined; (2) tumor, node, and metastasis (TNM) stage undefined; (3) unknown surgical treatment status; (4) presence or history of other primary malignancies; and (5) unknown survival time and/or cause of death. All cases were restaged by the 7th American Joint Committee on Cancer (AJCC) TNM staging system.

2.2. Statistical analysis

The gender, age, ethnicity, histological type, marital status, tumor grade, surgery data, TNM stage, cause of death, and survival time were extracted from the SEER database. Race was classified as white, black, or other. The tumor grades include high/moderate grade, poor/anaplastic grade, and unknown. Marital status was described as married, never married (single), divorced, widowed, or separated at the time of diagnosis. Separated and divorced patients were grouped together as the divorced/separated group. The primary endpoint of this study was cause-specific survival (CSS), which was calculated from the date of diagnosis to the date of cancer specific death. The longest follow- up for the cohort analyzed for CSS was 120 months.Deaths attributed to RC were treated as events and deaths from other causes were censored events. Rectum-specific surgery codes 10–90 were defined as surgery, whereas codes 00 were defined as non-surgical procedures.

Analysis methods used were: chi-squared test for baseline patient characteristics, Kaplan-Meier method for survival rates, and the multivariate Cox proportional hazards regression model for survival-associated risk factors as per marital status. The variable included in multivariate analysis were age, race, pathological grade, histotype, surgery, TNM stage, and marital status. The primary endpoint of this study was CSS, which was calculated from the date of diagnosis until the time of cancer-specific death. Deaths resulting from RC were treated as events and other causes were censored. All statistical analyses were performed using SPSS for Windows, version 23.0 statistical package. Two-sided $P < 0.05$ was accepted as statistically significant.

3. Results

3.1. Demographic and baseline patient characteristics

Baseline and pathological characteristics of patients are described in Table 1. We identified 27,498 eligible RC patients (16,399 men (59.6%); 11,099 women (40.4%)) from the SEER database. Among these, 16,356 (59.5%) were married, 3872 (14.1%) were widowed, and 4052 (14.7%) were never married at the time of diagnosis. Separated patients (312 (1.1%)) and divorced patients (2906 (10.6%)) were grouped under a divorced/separated group (3218 (11.7%)). The widowed group had more women, elderly (≥60 years), white, and early-stage (stage I/II) ($P < 0.001$) patients. Widowed patients were more susceptible to adenocarcinoma other than mucinous adenocarcinoma/signet ring cell carcinoma, and had a higher proportion of poor/anaplastic grade disease at diagnosis. Married (85.4%) patients were more likely to receive surgery compared to the widowed (76.6%), never married (74.1%) or divorced/separated (79.5%) patients ($p < 0.001$).

3.2. Impact of marital status on rectal cancer CSS

Univariate log-rank test was used to estimate 5-year CSS of RC patients. The overall 5-year overall survival (OS) rates were 71.9% for the married group, 56.5% for the widowed group, 58.0% for the never married group, and 63.4% for the divorced/separated group, and were significantly different ($P < 0.001$, Table 2, Fig. 1). Elderly age ($P < 0.001$), black race ($P < 0.001$), poor/anaplastic grade ($P < 0.001$), mucinous cancer and signet-ring cell cancer ($P < 0.001$), advanced TNM stage ($P < 0.001$), and no surgery ($P < 0.001$) prognosticated a poor 5-year CSS (Table 2).The 5-year CSS of men and women was not significantly different ($P = 0.851$). Further multivariate Cox regression analysis showed that age, race, pathological grade, histotype, surgery, TNM stage, and marital status were independent prognostic factors associated with CSS. Black patients had a higher risk of death from cancer than did white patients (hazard ratio (HR): 1.24, 95% confidence interval (CI): 1.16-1.33, $P < 0.001$, Table 2). Elderly patients (≥60 years) had worse CSS than younger patients (HR: 1.50, 95% CI: 1.43-1.56, $P < 0.001$, Table 2). Higher mortality rate was linked to poor/anaplastic grade compared to a high/moderate grade (HR: 1.50, 95% CI: 1.42-1.58, $P < 0.001$, Table 2), and to mucinous adenocarcinoma compared to adenocarcinoma (HR: 1.24, 95% CI: 1.13-1.35, $P < 0.001$, Table 2). Having no surgery led to worse CSS than receiving surgery (HR: 2.97, 95% CI: 2.82-3.22, $P < 0.001$, Table 2). Patients with advanced stage (stage II/III/IV) had higher mortality rate than did those at stage I (stage, HR, 95% CI: stage II, 1.86, 1.74-2.01; stage III, 2.84, 2.65-3.05; stage IV, 9.67, 9.00-10.39, Table 2). Compared to married patients, patients who were widowed (HR: 1.61, 95% CI: 1.51-1.70), never married (HR: 1.40, 95% CI: 1.33-1.49), or divorced/separated (HR: 1.16, 95% CI: 1.09-1.23) displayed poorer survival outcomes, after adjusting for demographics (Table 2).

3.3. Subgroup analysis by surgery status

We assessed the influence of marital status on survival at surgery or no surgery status. Marital status was an independent prognostic factor in the differences in receipt of surgery both in univariate and multivariate analysis ($P < 0.001$). Widowed patients had the lowest 5-year CSS in both surgery and no surgery groups. The 5-year CSS of widowed patients was 11.7% lower compared with married patients in the surgery group (79.4% vs. 67.7%, $P < 0.001$) and 9.2% lower compared to that of married patients in the no surgery group (25.5% vs. 16.3%, $P < 0.001$). In the surgery group, widowed (HR: 1.69, 95% CI: 1.56-1.82), never married (HR: 1.43, 95% CI: 1.33-1.54), and divorced/separated (HR: 1.25, 95% CI: 1.15-1.36) patients had a higher risk of RC mortality compared with married patients. However, compared with married patients, the mortality rate of divorced/separated patients (HR: 1.04, 95% CI 0.94-1.16, $P = 0.428$) was not different in the no surgery group (Table 3).

3.4. Subgroup analysis according to SEER stage

We then assessed the influence of marital status on survival at each tumor stage. Marital status was an independent prognostic factor in each tumor stage both in univariate and multivariate analysis ($P < 0.001$).Widowed, never married and divorced/separated patients had a consistently lower 5-year CSS compared with that of married patients at each stage (Table 4, Fig. 1). Widowed patients showed the lowest 5-year CSS, which was lower than that in married patients by 13.7% at stage I (91.0% vs. 77.3%, $P < 0.001$), 16.6% at stage II (81.1% vs 64.5%, $P < 0.001$), 20.3% at stage III (73.2% vs. 52.9%, $P < 0.001$), and 8.0% at stage IV (16.6% vs. 8.6%, $P < 0.001$). However, in multivariate analysis, divorced/separated patients were not likely to have a significantly higher risk of cancer-specific mortality