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Marital status and colon cancer outcomes in US Surveillance, Epidemiology and End Results registries: Does marriage affect cancer survival by gender and stage?

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ABSTRACT

Background: Marital status has been associated with outcomes in several cancer sites including breast cancer in the literature, but little is known about colon cancer, the fourth most common cancer in the US. *Methods*: A total of 127,753 patients with colon cancer were identified who were diagnosed between 1992 and 2006 in the US Surveillance, Epidemiology and End Results (SEER) Program. Marital status consisted of married, single, separated/divorced and widowed. Chi-square tests were used to examine the association between marital status and other variables. The Kaplan–Meier method was used to estimate survival curves. Cox proportional hazards models were fit to estimate the effect of marital status on survival. *Results*: Married patients were more likely to be diagnosed at an earlier stage (and for men also at an older age) compared with single and separated/divorced patients, and more likely to receive surgical treatment than all other marital groups (all $p < 0.0001$). The five-year survival rate for the single was six percentage points lower than the married for both men and women. After controlling for age, race, cancer stage and surgery receipt, married patients had a significantly lower risk of death from cancer (for men, HR: 0.86, CI: 0.82–0.90; for women, HR: 0.87, CI: 0.83–0.91) compared with the single. Within the same cancer stage, the survival differences between the single and the married were strongest for localized and regional stages, which had overall middle-range survival rates compared to in situ or distant stage so that support from marriage could make a big difference. *Conclusions*: Marriage was associated with better outcomes of colon cancer for both men and women, and being single was associated with lower survival rate from colon cancer.

1. Introduction

Decades of research has demonstrated that marriage has a strong, positive effect on human survival [1]. A recent meta-analysis of published studies shows a relative risk of mortality of 0.88 (95% CI: 0.85–0.91) for the married compared to the unmarried [2]. And in a large study of nearly 300,000 Americans, the protective effects of marriage are present for each non-married category (divorced/separated, widowed, and never-married) [3].

Marriage is likely the most important type of "social support," which has been linked to a variety of physiological mechanisms affecting health [4]. In addition to providing emotional support and access to social networks, the spouse also plays a critical role in monitoring and shaping health-related behavior [5,6].

General population-based mortality studies have mixed results when cancer is considered as a factor [1,3]. However, within the cancer patient population, the protective effect of marriage has been explored in the literature in a variety of cancer sites such as breast cancer, bladder cancer, cervical cancer, lung cancer and prostate cancer [7–16], and all but a few studies [9,16] find statistically significant survival benefits of marriage. The reasons that married cancer patients may have better outcomes include that married people are diagnosed at earlier stages [7,8], and are more likely to receive recommended treatment [7,17]. Early diagnosis and treatment compliance are consistent with the monitoring and behavior-shaping role that spouses often perform.

It is of interest to explore the relationship between marital status and colon cancer, since colon cancer is the fourth most common cancer in the US for both men and women, and marriage is a most important part of life for adults. Married people may have the above-mentioned health benefits, yet they may also have

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higher risk of obesity [18], which is a recognized risk factor for colon cancer. This study is among the few to address marital status and colon/colorectal cancer [17,19–22]. Except for Kvikstad et al. [19], all other studies have found a significant survival benefit for the married versus the single [20–22]. The study by Goodwin et al. [17] is the only one that has addressed the US population. However, their data were only from the state of New Mexico with the most recent data in 1982, and their study did not separate men and women, who have a very different marital pattern [23]. Our study uses data in 1992–2006 from the US Surveillance, Epidemiology and End Results (SEER) cancer registry program that covers 26% of US population, and is one of the largest studies on marriage and survival ever conducted on cancer patients. Rather than studying all cancers combined where too much aggregation across different diseases may affect the results [17,19–21], we focus on colon cancer for more detailed analysis in order to explore in what aspects marital status affects cancer survival. This paper also provides new insight into when marital status can make the biggest difference through sub-group analysis by cancer stage.

2. Patients and methods

2.1. Patients

This study used colon cancer patients diagnosed between 1992 and 2006 from 13 cancer registries in the SEER database. Colon cancer site was indicated by the following International Classification of Diseases for Oncology, Third Edition, (ICD-O-3) codes: C180–C189, and C260. We included all colon cancer patients who were aged 18 and above, had primary tumor in colon, and were reported to cancer registries by hospitals. Patients with missing information on marital status, age, race, cancer stage, or surgery receipt were excluded from our study. Since the marriage patterns by age for men and women were quite different (e.g., a much higher proportion of senior men are married than senior women) [23], survival analysis was done for each gender group separately.

2.2. Statistical methods

Analysis of variance (ANOVA) was used to compare mean age at diagnosis across marital status. Chi-square tests were conducted to test the association between two categorical variables. Since only primary colon cancer was considered, death from cancer in survival analysis was defined as death from any cancer site. The Kaplan–Meier method was applied to estimate 5-year survival rates. Log-rank tests were used to compare the difference of survival curves by marital status. Cox proportional hazard models were fit to estimate the effect of marital status on the risk of death from cancer, after controlling for age, cancer stage, race and surgery receipt. To explore how marital status affects patients diagnosed at the same stage, subgroup analysis was done by cancer stage.

3. Results

We identified 127,753 colon patients from SEER data, among whom 11.7% were single (i.e., never married), 56.6% were married, and 23.6% were widowed. The 0.7% separated plus the 7.4% divorced were grouped together as the divorced/separated group in our study. Marital status composition was considerably different between male and female patients by Chi-square test ($p < 0.0001$), consistent with the US general population [23]. For instance, among married colon cancer patients, 60% were men; whereas among the widowed, only 19% were men.

Patient characteristics for men and women are presented in Tables 1 and 2, respectively. The mean age for married men was much higher than that for the single and the separated/divorced ($p < 0.0001$). The median age at diagnosis for married men was 69, whereas it was 62 for the single and 63 for the separated/divorced (Table 1). However, for women, the median and the mean age were similar for the married, the single, and the separated/divorced (Table 2). Unsurprisingly the widowed had an older age for both men and women.

The SEER historic stage (in situ, localized, regional and distant) was used in the analysis, which is consistently defined over time by the SEER program. Married people were more likely to be diagnosed at an earlier stage, and less likely to be diagnosed at distant stage compared to the single and the separated/divorce ($p < 0.0001$). Of married men, 22.2% were diagnosed at distant stage, while 28.6% single men and 28.6% separated/divorced men were diagnosed at distant stage (Table 1). For married women, 21.8% were diagnosed at distant stage, while 25.0% of single women and 24.4% of separated/divorced women were diagnosed at distant stage (Table 2).

The married were also more likely to receive surgery ($p < 0.0001$). Surgery was received by 93.2% of married men, 88.5% of single men, and 89.2% of separated/divorced men, even though married men were about 6–7 years older in median age (Table 1). A higher proportion of married women (94.6%) had surgery than women in other marital groups with a proportion ranging from 90.5% through 92.6% (Table 2).

The Kaplan–Meier survival curves for men and women are presented separately in Fig. 1. Log-rank tests showed married

Table 1
Patient characteristics by marital status for men.

Variable	Single (n = 7407, 12.2%)	Married (n = 43,134, 71.1%)	Separated/divorced (n = 4389, 7.2%)	Widowed (n = 5715, 9.4%)	p-Value
Age, years					
Mean ± sd	60.9 ± 15.2	67.2 ± 12.3	63.2 ± 11.4	78.2 ± 9.0	<0.0001
Median	62	69	63	79	
Race, %					<0.0001
White	71.9	81.6	77.2	83.0	
Black	18.6	7.5	16.0	9.4	
Other	9.5	10.9	6.8	7.6	
SEER summary stage, %					<0.0001
In situ	5.1	5.4	4.6	4.1	
Localized	30.6	35.9	30.2	35.6	
Regional	35.7	36.5	36.5	37.3	
Distant	28.6	22.2	28.6	22.9	
Surgery, %					<0.0001
Yes	88.5	93.2	89.2	89.6	
No	11.6	6.8	10.8	10.4	

Table 2
Patient characteristics by marital status for women.

Variable	Single (n = 7598, 11.3%)	Married (n = 29,137, 43.4%)	Separated/divorced (n = 5976, 8.9%)	Widowed (n = 24,400, 36.4%)	p-Value
Age, years					
Mean ± sd	65.4 ± 16.3	65.7 ± 12.8	65.3 ± 12.4	79.3 ± 8.9	<0.0001
Median	67	67	66	80	
Race, %					<0.0001
White	69.5	80.1	73.8	82.6	
Black	22.7	8.1	20.4	9.9	
Other	7.8	11.8	5.8	7.5	
SEER stage, %					<0.0001
In situ	4.8	4.6	5.0	3.4	
Localized	32.1	34.9	31.8	35.1	
Regional	38.2	38.8	38.7	39.8	
Distant	25.0	21.8	24.4	21.7	
Surgery, %					<0.0001
Yes	91.1	94.6	92.6	90.5	
No	8.9	5.4	7.4	9.5	

people (the uppermost line) had better survival than all the other marital groups ($p < 0.0001$) for both men and women. For male patients, the five-year survival rate was 59% for single, 65% for married, 56% for separated/divorced and 57% for widowed. For female patients, the five-year survival rate was 61% for single, 67% for married, 59% for separated/divorced and 62% for widowed. The five-year survival rate for the single compared to the married was six percentage points lower for both men and women.

Results from Cox proportional hazard models are shown in Table 3. Marital status was a significant predictor of risk of death from cancer ($p < 0.0001$) for both men and women. This prognostic effect was independent of age, race, cancer stage, and having surgery (all $p < 0.0001$). Compared with the single, the married had a lower risk of death from cancer (for men, HR: 0.86, 95% CI: 0.82–0.90, $p < 0.0001$; for women, HR: 087, 95% CI: 0.83–0.91, $p < 0.0001$); and the divorced/separated or the widowed were not statistically different from the single (p ranged from 0.38 to 0.62). Increasing age, being black, having more advanced cancer stage, and having no surgery were associated with higher risk of death from cancer (all $p < 0.0001$).

As has been shown previously (Tables 1 and 2), married people were more likely to be diagnosed at an earlier stage; but among patients of the same cancer stage, was there a protective marital effect? To explore this, subgroup analysis within the same stage was conducted. As shown in Fig. 2(b and c), five-year survival rates for married people were considerably higher than all other marital groups for localized and regional stages for both men and women. For instance, married women had 90% 5-year survival rate whereas single women had just 85% in localized stage; for regional stage, the 5-year survival was 70.8% for married women and 64.2% for single women. However, the five-year survival rates for married people were not much different from the single or the separated/divorced (or at least not monotonously higher) for both men and women at in situ and distant stages (Fig. 2a and d). The 5-year survival rates were within two-percentage-point difference across married, single and divorced/separated at in situ and distant stages. These patterns may be attributable to the fact that the in situ and the distant stage had survival rates that were either too low (in situ) or too high (distant) so that the protective effect of marriage was not visible; whereas localized and regional stages

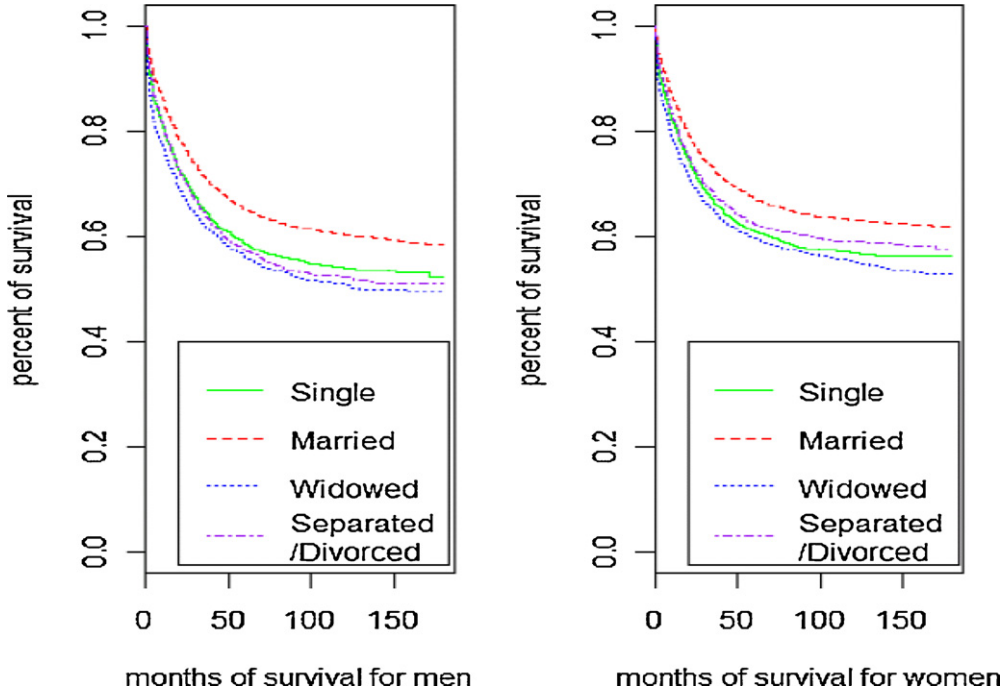

Fig. 1. Kaplan–Meier plots of survival curves by marital status.

Table 3
Hazard ratios of risk of death by Cox proportional hazard model.

Variable	Men			Women		
	HR	95% C.I.	*p*	HR	95% C.I.	*p*
Age in years	1.02	1.020, 1.022	<0.0001	1.02	1.018, 1.020	<0.0001
Race (ref: white)						
Black	1.18	1.13, 1.24	<0.0001	1.15	1.10, 1.20	<0.0001
Other	0.87	0.83, 0.91	<0.0001	0.90	0.86, 0.95	<0.0001
Marital status (ref: single)						
Married	0.86	0.82, 0.90	<0.0001	0.87	0.83, 0.91	<0.0001
Separated/divorced	0.98	0.92, 1.04	0.52	0.99	0.93, 1.05	0.62
Widowed	1.02	0.96, 1.08	0.51	0.98	0.93, 1.02	0.38
Stage (ref: localized)						
In situ	0.25	0.20, 0.32	<0.0001	0.29	0.23, 0.36	<0.0001
Regional	3.80	3.61, 4.00	<0.0001	3.65	3.48, 3.82	<0.0001
Distant	20.16	19.16, 21.21	<0.0001	19.33	18.42, 20.28	<0.0001
Surgery (ref: yes)						
No	2.90	2.78, 3.01	<0.0001	2.94	2.83, 3.06	<0.0001

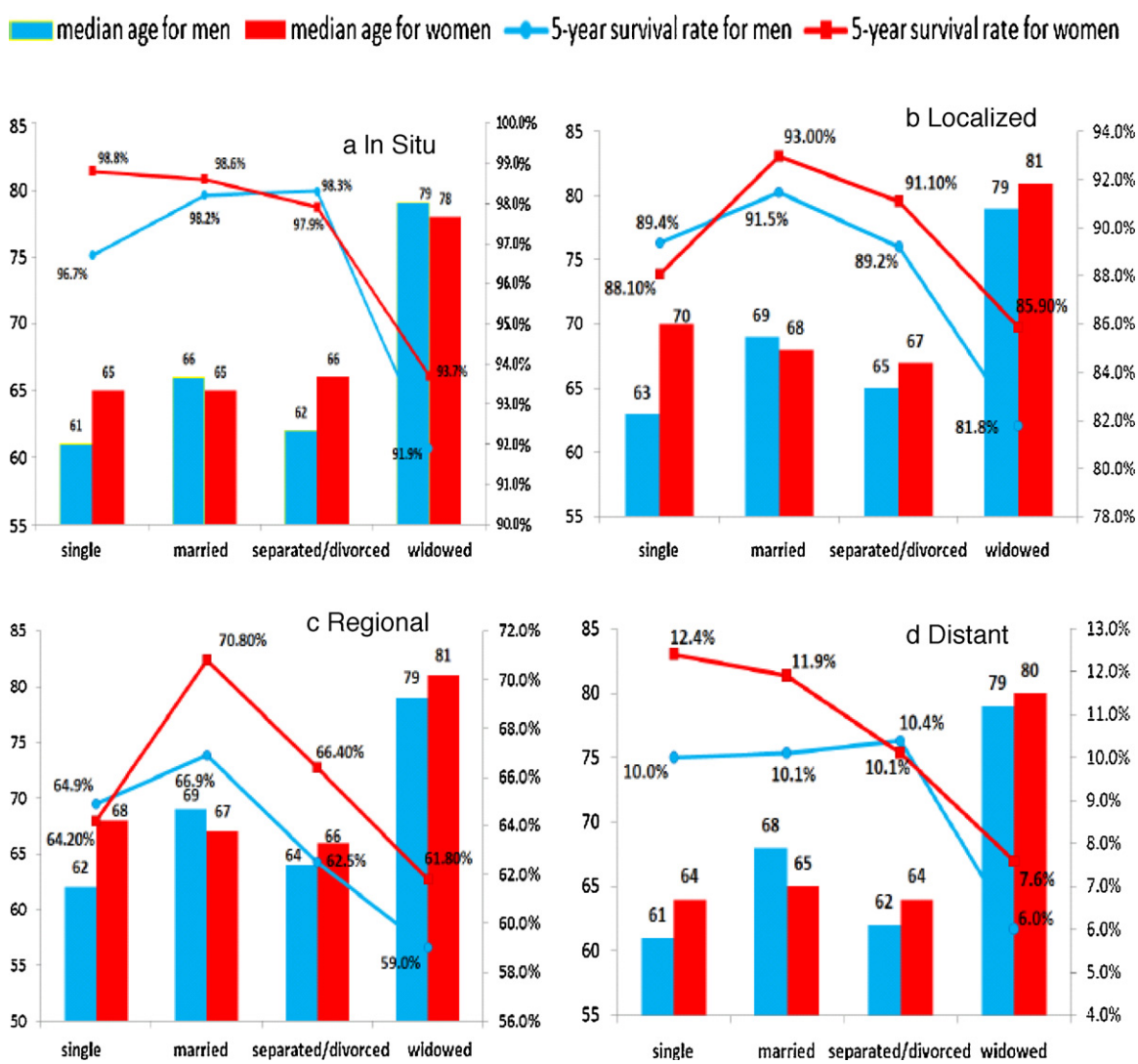

Fig. 2. Age at diagnosis and five-year survival rates by gender, stage and marital status.

had middle range survival rates so that support from marriage could make a substantial difference.

Fig. 2 also indicated that married men were likely to be diagnosed at a much older age (4–7 years higher in median age) than single men or divorced/separated men for all cancer stages. Being diagnosed at an older age may be attributed to two opposing effects: the delay of disease onset or the delay to detect disease. However, given that married men were less likely to be diagnosed at distant stages than the single and the separated/divorced men, a diagnosis at an older age for married men should be more indicative of later disease onset. Women, be married, single or divorced/separated, were diagnosed at about the same age, suggesting that the marital protective effect of later disease onset for women may not be as big as that for men.

4. Discussion

Explanations for the relationship between health and marital status are often put into two categories. One category consists of selection effects because marital transitions may be, in part, a result of health: people in robust health may be more likely to get married and stay married. These selection effects are often just hypothesized rather than tested, but some research suggests that health affects marital transitions [24–26].

The other category of explanations for a marriage effect on health outcomes emphasizes marriage as a means of social support. The analysis in this study provides important confirmation of the social support hypothesis. This study confirms previous research that married individuals have significantly earlier cancer diagnosis, which is consistent with the spousal health monitoring hypothesis mentioned previously. Furthermore, the higher probability of surgery suggests that spouses help encourage patients to pursue more aggressive (and in this case highly beneficial) treatment options, perhaps because having a committed life partner gives patients more to live for. Though, the SEER data do not provide information on cancer screening test, earlier diagnosis for married people may suggest a higher likelihood of married people getting screened.

An important aspect of this study is the ability to control for the stage of cancer progression at baseline. The wide array of demographic studies on all-cause mortality seldom have the ability to do this and are, consequently, highly subject to the selection effects just described, though a richer set of health-related control variables than are available in SEER would be desirable to provide a more accurate picture of baseline health.

This study also contributes to the debate on whether marriage is equally protective for men as it is for women. Earlier studies led to a persistent and widely held view that the health benefits from marriage are much larger for men than for women [27–29]. This study has mixed findings. In terms of diagnosis, men benefited more than women in two ways. First, married men were diagnosed at a much older age than the single or the separated/divorced, whereas there was no such big age difference in women. Second, the chance of being diagnosed at distant stage was about 6 percentage points lower for married men compared the single and the separated/divorced, whereas it was just about 3 percentage points lower for married women (Tables 1 and 2). However, after colon cancer diagnosis, women tend to benefit more from family support in that the survival difference between the married and the single was more than five percentage points for women diagnosed in local or regional stage; whereas it was just about two percentage point for men (Fig. 2).

An obvious limitation of the SEER data is the relative lack of control variables beyond simple demographics. In particular, the lack of education, wealth, and socioeconomic status variables are key limiting factors. For example, economic deprivation is found to be associated with colon cancer survival [30]. However, the many studies on all-cause mortality that typically do have controls for these additional variables consistently find large and significant marriage effects. Additionally, many of these additional risk factors might be simply mediating effects that have marital status as an underlying cause.

There is also lack of marital transition information in the SEER data. We observe marital status only at baseline, making it impossible to treat marital status as a time-varying covariate. However, the lack of marital transitions (meaning marital status may actually be "mis-classified" prior to death or the end of the study) has been shown to actually diminish the estimated protective effect of marriage [31]. For older individuals who have cancer, by far the most prominent unobserved marital transition will be transition from being married to being either widowed or separated/divorced (as opposed to transitions into marriage). Therefore, the protective effect of marriage would be likely even larger if marital status transitions were included in the survival analysis.

As is common with observational studies, there is often missing information on variables of interest. However, fortunately, the SEER program is considered the standard for data quality around the world, thanks to its routine and rigorous data quality control measures [32]. The variables in this study are all well-populated in the SEER data: only about 4% patients were excluded from our study for unknown marital status; and another combined 3% were excluded for all the other variables considered. The degree of missing information is rather mild given the large sample size. Nevertheless, we also conducted a worst-case scenario sensitivity analysis, where all missing marital status was assigned to one marital status. No matter which marital status they were assigned to, the marital effects found in this paper remained the same.

Given that being married is associated with better outcomes from colon cancer, additional research is needed to determine the underlying causes of the survival benefits. For example, this may be explained by more social and psychological support for married couples as well as their potentially healthier eating habits. Marital status can be a predictor of cancer survival, and additional social and community support is needed for unmarried cancer patients due to their higher risks.

Conflict of interest statement

The authors report no conflict of interests.

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