

limited by old database or queried from the Surveillance, Epidemiology, and End Results (SEER) database which was lack of certain important information such as adjuvant chemotherapy, or clinic-pathologic predisposing factors that could influence survival. Thus, we have chosen to investigate the effect of marital status on survival among patients with surgically treated colon cancer.

2. Methods

2.1. Ethical statement

Because we did not use any human subjects or personal identifying information records in our analysis, informed consent was not required. The study protocol was approved by the Ethics Committee of the Institutional Review Board of the Chi-Mei medical center (IRB: CMFHR10707-012).

2.2. Patient demographics and database

The data for this study were collected from the cancer registry dataset in the Chi-Mei medical center between January 1, 2010 and December 31, 2015. Electronic medical records and a cancer registry dataset were retrospectively reviewed. All patients were regularly monitored after diagnosis until death or last follow-up date. In this study, follow-up was completed on April 30, 2018. Finally, a total of 925 patients with colon cancer who underwent curative surgery with or without adjuvant therapy in accordance with National Comprehensive Cancer Network (NCCN) guidelines were identified for this study. Rectal cancer was not included in this analysis because it frequently is treated with a different sequence, such as neoadjuvant chemoradiotherapy. Exclusion criteria included the following: a previous history of cancer, age <18 years, chemotherapy as the initial treatment, or incomplete data. Our cancer registry dataset provided information on the following: date of diagnosis, age, sex, personal habits, circumferential resection margin (CRM), lymph node count, tumor grade, perineural invasion (PNI), adjuvant treatment (e.g., chemotherapy), clinical/pathologic American Joint Committee on Cancer (AJCC) stage and cause of death. All staging were according to the AJCC cancer staging (7th edition). Marital status was captured at the time of diagnosis and was classified in a binary fashion as married or unmarried category (never-married, separated, divorced, or widowed). The clinical end point was 5-year disease-specific survival (DSS) rate. Deaths due to cancer were recorded as events and deaths secondary to other causes, at 5 years following diagnosis or the last follow up date were recorded as censored.

2.3. Statistical analysis

All statistical operations were performed using SPSS statistical software (version 20, SPSS Inc; Chicago, IL). All *P*-value are calculated from 2-sided and the threshold of 0.05 was set for statistical significance. All confidence intervals (CIs) are stated at the 95% confidence level. Continuous variables were compared with one-way analysis of variance (ANOVA), and category variables were analyzed with Pearson chi-square test or Fisher exact test. The 5-year DSS rate is described by the Kaplan–Meier method, and the differences were compared using log-rank statistics. Multivariate Cox regression model was used to evaluate the effect of marital status on disease-specific survival rates after adjusting for other confounding variables. Stratified survival analyses were also performed on particularly different groups.

Table 1

Demographic, clinical, and pathological characteristics in operated colon cancer patients to marital status, n=925.

Variable	Married n = 749 n (%)	Unmarried n = 176 n (%)	<i>P</i> value
Age at diagnosis (Mean ± SD)	65 ± 12	64 ± 16	.272
≤65 y	388 (51.8)	83 (47.2)	.268
>65 y	361 (48.2)	93 (52.8)	
Gender			<.001
Male	454 (60.6)	77 (43.8)	
Female	295 (39.4)	99 (56.3)	
Lymph node count			.782
≤12	88 (11.8)	22 (12.5)	
>12	661 (88.3)	154 (87.5)	
T category			.040
T1-2	138 (18.4)	21 (11.9)	
T3-4	611 (81.6)	155 (88.1)	
N category			.345
N0	353 (47.1)	76 (43.2)	
N1–2	396 (52.9)	100 (56.8)	
Stage			.085
Stage I–II	343 (45.9)	68 (38.6)	
Stage III–IV	406 (54.2)	108 (61.4)	
Grade			.042
Well/moderately	642 (85.7)	140 (79.6)	
Poorly/undifferentiated	107 (14.3)	36 (20.5)	
Perineural invasion			<.001
No	555 (74.1)	107 (60.8)	
Yes	194 (25.9)	69 (39.2)	
Circumferential resection margin			.490
Negative	708 (94.5)	164 (93.2)	
Positive	41 (5.5)	12 (6.8)	
Adjuvant treatment			.585
Nil	289 (38.6)	64 (36.4)	
CT/RT	460 (61.4)	112 (63.6)	
Personal habits			.848
Nil	578 (77.2)	137 (77.8)	
Cigarette/or alcohol use	171 (22.8)	39 (22.2)	

CT/RT=chemotherapy and/or radiotherapy.

3. Results

3.1. Demographic characteristics

The demographic, clinical, and pathological characteristics of this study are displayed in Table 1. A total of 925 patients were identified, with 531 men (57.4%) and 394 women (42.6%). The median follow-up for the cohort analyzed was 39.1 months (range, 1–85.8). Among these patients, 749 (80.9%) were married, and 176 were unmarried (19.1%) including 42 who were never married (4.5%), 42 were divorced/separated (4.5%), and 93 were widowed (10.1%). The mean age was 65 ± 12 years for married patients and 64 ± 16 years for unmarried patients. Unmarried patients were more likely in female patients and presented with worse tumor behavior such as advanced tumor category, poorly/undifferentiated, and PNI than married patients (all, *P* < .05); however, there was no significant difference between the married and unmarried groups in cancer stage and the rate of receiving adjuvant treatment. The Kaplan–Meier survival curve was generated to compare the 5-year DSS. As presented in Fig. 1, the 5-year DSS differed significantly among married and unmarried subgroups. Log-rank tests showed married patients had better survival outcome compared with

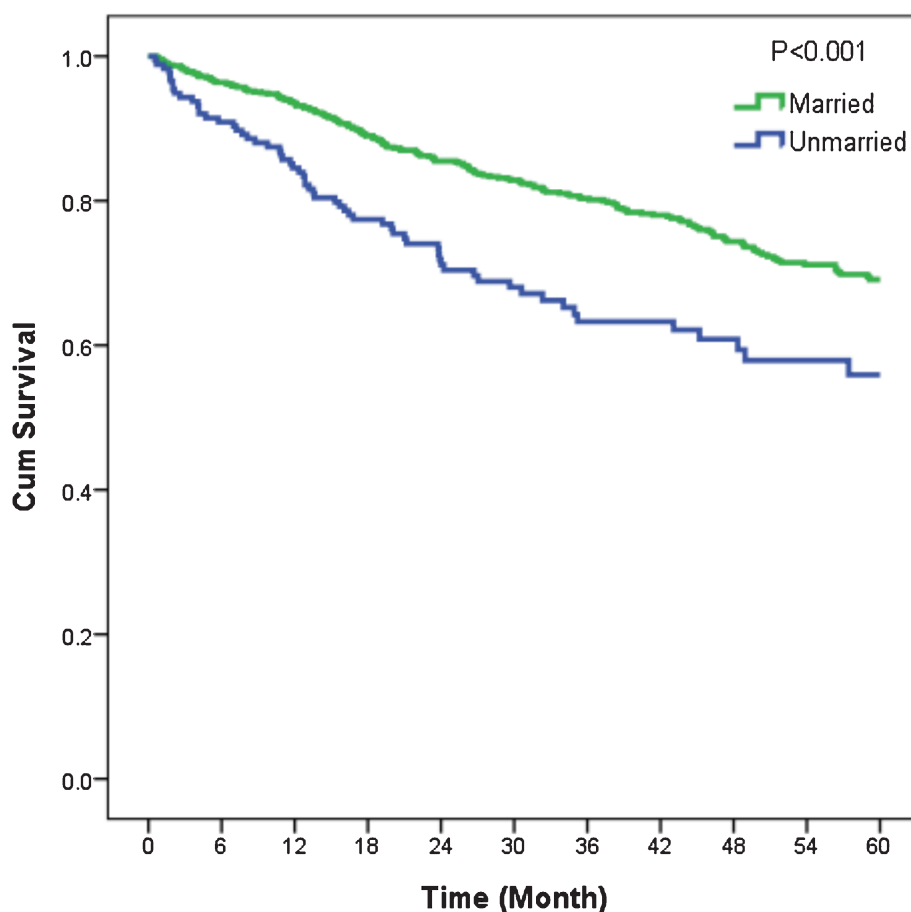


Figure 1. The 5-year disease-specific survival was 69.1% in the married group and 55.9% in the unmarried group among surgically treated colon cancer patients ($P < .001$).

unmarried patients (69.1% vs 55.9%, $P < .001$). Additionally, age >65 years, unmarried status, advanced stage, lymph node yield <12, poorly/undifferentiated histology, positive CRM, PNI, and without adjuvant therapy were identified as significant risk factors for poor survival on univariate analysis (Table 2). On multivariate analysis shown in Table 3, all of these variables were validated as independent prognostic factors including unmarried status (adjusted HR [aHR], 1.66; 95% CI, 1.24–2.22). Then we performed stratified analysis for 5-year DSS according to different demographic variables. In Table 4, unmarried status was a significant negative factor in the age group >65 years (HR 1.93, 95% CI: 1.35–2.75), in the female group (HR 2.89, 95% CI: 1.96–4.29), in the group with well/moderately differentiated tumor (HR 1.81, 95% CI: 1.29–2.54), and in the group with advanced stage disease (III–IV) (HR 1.77, 95% CI: 1.28–2.45).

4. Discussion

The aim of this study was to investigate the impact of marital status on the survival of patients with surgically treated colon cancer. Our results demonstrated that married patients had better 5-year DSS compared with unmarried patients. These findings remained significant after inclusion of all demographic, clinic-pathologic, and treatment variables in a fully adjusted Cox regression model. Further-stratified analysis revealed that married patients experienced a significant benefit of 5-year

DSS in the subgroups of age >65 years, female sex, well/moderately differentiated tumor, and advanced stage disease (III–IV) than the unmarried.

This study has several strengths. First, patients in our study were treated at a single institution, and underwent surgery as routine clinical practice. Treatment was not likely to have differed

Table 2
Univariate analysis for the 5-year disease-specific survival, n = 925.

	HR (95% CI)	P value
Age at diagnosis	1.03 (1.02–1.04)	<.001
≤65 y	1	
>65 y	1.86 (1.44–2.41)	<.001
Gender: Female	1.01 (0.78–1.30)	.961
Marital status: Unmarried	1.83 (1.37–2.44)	<.001
Lymph node count: >12	0.64 (0.45–0.90)	.009
T category: T3–4	2.96 (1.83–4.79)	<.001
N category: N1–2	3.13 (2.34–4.12)	<.001
Stage: Stage III–IV	3.95 (2.89–5.39)	<.001
Grade: poorly/undifferentiated	1.99 (1.48–2.66)	<.001
Perineural invasion: yes	2.36 (1.83–3.05)	<.001
Circumferential resection margin: positive	2.85 (1.95–4.18)	<.001
Adjuvant treatment: CT/RT	1.32 (1.01–1.72)	.041
Personal habits: cigarette/or alcohol use	1.04 (0.78–1.40)	.785

CI=confidence interval, HR=hazard ratio, RT/CT=chemotherapy and/or radiotherapy.

Table 3
Multivariate analysis for the 5-year disease-specific survival, n=925.

	Model A		Model B	
	HR (95% CI)	P value	HR (95% CI)	P value
Age at diagnosis:>65 y	1.77 (1.37–2.30)	<.001	1.76 (1.36–2.29)	<.001
Marital status: unmarried	1.66 (1.24–2.22)	.001	1.65 (1.23–2.20)	.001
Lymph node count: >12	0.49 (0.35–0.70)	<.001	0.52 (0.37–0.68)	<.001
T category:T3–4	1.88 (1.12–3.16)	.017		
N category: N1–2	2.98 (2.15–4.16)	<.001		
Stage: Stage III–IV			4.52 (3.17–6.34)	<.001
Grade: poorly/undifferentiated	1.94 (1.44–2.60)	<.001	1.96 (1.46–2.64)	<.001
Perineural invasion: yes	1.65 (1.26–2.17)	<.001	1.66 (1.27–2.17)	.001
Circumferential resection margin: positive	2.38 (1.61–3.52)	<.001	2.51 (1.70–3.71)	<.001
Adjuvant treatment: CT/RT	0.64 (0.47–0.86)	.003	0.59 (0.44–0.79)	.001

CT/RT = chemotherapy and/or radiotherapy.

between married and unmarried patients. Second, our database provides important information on the predisposing factors that could influence survival (e.g., factors such as tobacco use and alcohol consumption, CRM status, and adjuvant chemotherapy). We could perform an in-depth assessment of the impact of these factors on outcome. Third, we included patients with surgically treated colon cancer diagnosed between January 1, 2010 and December 31, 2015. Thus, our study is more reflective of current conditions that differ from the conditions characteristic of previous studies. Finally, the use of a statistical method such as stratified analysis was accurate for survival prediction and classification. Therefore, this prognostic stratification regarding the effect of marital status on outcomes in surgically treated colon cancer could assist clinicians in further therapeutic selections.

The association between married status and improved outcome has been identified in many studies.^[14–16] A common explanation for the relationship is that marriage is a source of social support. Spouses may encourage their partners to undergo cancer screening, complete recommended treatment, and receive more intensive therapy. In addition, a spouse may influence the patient’s health-related behavior, such as encouraging the patient to quit cigarette smoking or to curtail excessive alcohol use.^[16–18] Furthermore, some studies also demonstrated that a partner could provide emotional support, reduce the stress response, and ease financial strain.^[19] Thus, married patients often have

a lower risk of depression than do unmarried patients.^[20] As a result, marital status provided protective effect to reduce cancer mortality and should be considered for improvement of cancer care.

Numerous published studies have observed that unmarried patients are at significantly higher risk of late stage diagnosis, under-treatment, and cancer-related death^[16,21]; however, our results revealed no significant difference between married and unmarried patients with colon cancer in cancer stage or the receipt of adjuvant therapy. One possible explanation is that we included only those patients who underwent curative tumor resection. Those patients who had precancerous lesions such as polyps, who may have been encouraged by their spouses to seek early cancer detection, treatment, and regular follow-up, may not have been included in our analysis. In addition, some patients who developed very advanced or metastatic disease due to delayed diagnosis who, therefore, could not have been treated by curative resection may also not have been included in our study. Moreover, this cancer registry database includes only those patients who have received a medical opinion at our medical center. It is plausible that it may have resulted in some degree of bias in favor of patients endowed with strong social support and family ties and favorable socioeconomic status, all of which enabled them to seek care at a tertiary medical center and perhaps may have obscured the previously reported benefits of marriage.

It is noteworthy that our findings are consistent with those of other studies in which married patients had the greatest reduction in cancer-related death in colon cancer.^[9,11] Aizer et al^[16] found significant cancer-specific survival benefit of marital status on colorectal cancer. Wang et al^[9] also reported that marriage has a protective effect on colon cancer survival. Married patients were more likely to be diagnosed at an earlier stage and more likely to receive surgical treatment than all other groups of non-married patients (all $P < .0001$). The 5-year survival rate for never-married patients was 6% lower than that of married patients. After controlling for confounders, married patients still had a significantly lower risk of death from cancer compared with never-married patients. Therefore, marital status should be recommended as an important social support strategy for colon cancer and additional social support for unmarried patients may lead to improve outcomes. For doctors, more health education is needed to influence the personal habits such as encouraging to quit smoking or excessive alcohol use.^[22] For healthcare systems, targeting single patient with regular screening, disease awareness programs, maintaining vigilance during surveillance, and offering

Table 4
Stratified analysis of marital status for the 5-year disease-specific survival according to age, gender, grade, and TNM stage n=925.

	HR (95% CI)	P value
Age at diagnosis		
≤65 year: unmarried	1.58 (0.96–2.60)	.069
>65 year: unmarried	1.93 (1.35–2.75)	<.001
Gender		
Male: unmarried	1.05 (0.65–1.71)	.831
Female: unmarried	2.89 (1.96–4.29)	<.001
Grade		
Well/moderately: unmarried	1.81 (1.29–2.54)	.001
Poorly/undifferentiated: unmarried	1.59 (0.91–2.77)	.104
Stage		
Stage I–II: unmarried	1.83 (0.96–3.51)	.068
Stage III–IV: unmarried	1.77 (1.28–2.45)	.001

CI = confidence interval, CT/RT = chemotherapy and/or radiotherapy, HR = hazard ratio.

psychological counseling are possible interventions that may mitigate this phenomenon.^[23] For governments, the investments in social support services and public insurance aiming at the widowed population could improve the likelihood of achieving cure.^[24]

This study had some limitations that should be addressed. First, potential confounding factors adversely affecting the health of cancer patients such as comorbidities reflecting poor general health and nutritional status, and postoperative complications could not be corrected in our analyses. As we know, comorbid conditions can impact the survival of colon cancer patients, which can lead to the development of non-cancer-associated competing mortality especially for those undergoing major surgery.^[25] In this study, only surgically treated colon cancer patients were included in this study; it means that those patients not suitable for surgery due to severe comorbidities were not enrolled in our analysis. The use of an instrumental variable analysis may help control measured and unmeasured confounding factors.^[26] Second, some detailed demographic data such as financial status, insurance status, and education which are related to social support cannot be obtained in our database^[27]; however, many of these additional risk factors might be simply mediating effects related to marital status. Finally, we recorded marital status only at the time of cancer diagnosis. Marital status could have changed during the study period; transition from being married to being unmarried is the most likely. In this case, the estimated effect of marriage could be larger than we observed in the survival analysis.^[9] Further research on marriage period and survival benefit is needed to clarify the details of this association.

Despite the stated limitations, our study has yielded conclusive results regarding the association between marital status and outcome of surgically treated colon cancer. Compared with unmarried patients, married patients had better 5-year DSS. Marriage is an independent predictor of improved survival in patients with colon cancer due to increased social and psychological support. Further interventions such as social and psychiatric referral may be considered to improve outcomes for unmarried patients, who are at greater risk.

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