

Effect of marital status on duodenal adenocarcinoma survival: A Surveillance Epidemiology and End Results population analysis

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Abstract. Numerous studies have shown that marital status may be a prognostic factor in various malignancies, but little is known about its effect on duodenal adenocarcinoma. The aim of the present study was to determine the association between marital status and survival in patients with duodenal adenocarcinoma. The Surveillance, Epidemiology and End Results database was utilized to analyze 2,018 patients who had been diagnosed with duodenal adenocarcinoma between January 2004 and December 2015. Kaplan-Meier and Cox regression analyses were also used to determine the impact of marital status on overall survival (OS) and cause-specific survival (CSS). The 5-year OS rate was higher in married patients (32.6%) compared with unmarried (26.8%) patients ($P < 0.001$), as was the 5-year CSS rate (38.8 vs. 33.7%; $P < 0.001$). Multivariate analysis demonstrated that marital status was an independent prognostic factor for duodenal adenocarcinoma, with married patients having improved OS ($P < 0.001$) and CSS ($P = 0.001$) compared with unmarried patients. Subgroup analysis showed that marital status played a role in the survival of patients at American Joint Committee on Cancer Tumor-Node-Metastasis stage I, but not of patients

at stages II, III or IV. The survival outcomes for duodenal adenocarcinoma are improved in married patients compared with those in unmarried patients. Therefore, attention should be paid to the impact of social factors and socio-economic factors on unmarried patients, in order to improve their survival outcomes.

Introduction

Duodenal adenocarcinoma that originates in the mucosal epithelium is the most common type of duodenal tumor and in 2014 accounted for 15-25% of cases of cancer of the small intestine in the United States (1). However, <1% of all cases of gastrointestinal cancer are diagnosed as duodenal adenocarcinoma, and this may be due to the duodenum being the shortest part of the small intestine (2,3). The primary treatment for duodenal adenocarcinoma is surgery, with pancreatoduodenectomy and segmental resection being the most commonly used (4). The rarity of this condition means that there is no consensus about the best adjuvant treatment strategy (5), and the scope of resection for duodenal adenocarcinoma remains controversial (6). Previous studies have suggested that regional lymph node metastasis is associated with lower survival rates in patients with duodenal adenocarcinoma (7-9). However, prognostic factors such as age, sex, tumor size, pathology grade and American Joint Committee on Cancer (AJCC) Tumor-Node-Metastasis (TNM) stage were not consistent with that result (10). Furthermore, relatively little is known about the effect of marital status on the outcome of duodenal adenocarcinoma, and the data that is available may be affected by the small sample size (11).

Extra emphasis is now being placed on the role of social determinants in disease development (12). Social support forms an important part of patient screening, treatment and follow-up care. It has been suggested that spouses tend to encourage early screening and adherence to treatment, thereby improving outcomes (13). Therefore, the potential importance of social conditions should not be ignored in patients with duodenal adenocarcinoma, especially given that married patients reportedly have improved survival outcomes in breast,

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ovarian, colon, and head and neck cancer (11,14-16). According to a previous study based on information in the Surveillance, Epidemiology and End Results (SEER) database, married patients are more likely to be diagnosed with earlier stages of cancer and therefore, the treatment regimens may be more effective compared with those in unmarried patients (11).

The aim of the present study was to elucidate the effects of marital status on the prognosis of patients with duodenal adenocarcinoma. The study investigated the impact of marital status on both overall survival (OS) and cause-specific survival (CSS) by analyzing demographic data obtained from the SEER database.

Materials and methods

Patient population and study design. Sponsored by the National Cancer Institute, the SEER program collects demographic, clinicopathological and survival data on a per-patient basis from 18 cancer registries across the United States, Hawaii and Alaska (17). The SEER database (<https://seer.cancer.gov/seerstat/software/>) was used to identify 2,018 patients with adenocarcinoma of the duodenum diagnosed between January 2004 and December 2015. Primary cancer site and histology were coded according to the criteria in the third edition of the International Classification of Diseases for Oncology (18). Major loci and morphological code C17.0 were used to define tumors localized to duodenum, and the histological recode broad groupings were used to identify the nature of the tumor. Codes 8140-8389 were used to define adenomas and adenocarcinomas. Patients were excluded if the duodenal adenocarcinoma was not the first primary tumor, the marital status was unknown, the age at diagnosis was <18 years or there was missing information on ethnicity, pathological grade, surgery, AJCC TNM stage or follow-up time. The primary outcomes of the present study were OS and CSS, which were defined as time until death from any cause and time until death caused by duodenal adenocarcinoma after diagnosis of duodenal adenocarcinoma, respectively. Death attributed to duodenal adenocarcinoma was regarded as an event. Patients who died from other causes or were still alive at the end of the last follow-up in December 2015 were treated as censored observations.

Study variables. The demographic and clinicopathological data were extracted from the SEER database, including year of diagnosis, age, sex, ethnicity, marital status, pathological grade, AJCC TNM stage and surgery versus no surgery. Patients were divided into three groups according to the age at diagnosis (≤ 58 , 59-75 and >75 years), into four groups according to the year of diagnosis (2004-2006, 2007-2009, 2010-2012 and 2013-2015) and into three groups according to ethnicity (Caucasian, African descent and others). The AJCC TNM stage was established according to the criteria described in the 6th edition of the AJCC Cancer Staging Manual (19), and as this staging system was publicly released in 2004, the study was limited to patients diagnosed between 2004 and 2015. Marital status is coded in the SEER database as married, divorced, widowed, separated, never married, or domestic partner. The codes were combined by classifying patients as either married (including married and domestic partner) or

unmarried (including never married, unmarried, divorced, separated and widowed).

Statistical analysis. Patient characteristics between the two groups were compared, and it was determined whether the continuous variables conformed to a normal distribution; those that did are expressed as the mean \pm SD, whereas those that did not are expressed as median values with the 25 and 75th percentiles provided. Continuous variables with a normal distribution were statistically compared using Student's t-test. Continuous variables that were not normally distributed were statistically compared using a Mann-Whitney U test. The categorical variables were compared using Pearson's χ^2 test. OS and CSS were calculated using Kaplan-Meier plots method and a log-rank test was used to compare differences between the groups in the Kaplan-Meier plots. A Cox proportional-hazards model was constructed to identify factors that were independently associated with the prognosis. Cox multivariate analysis included age as a categorical variable (≤ 58 , 59-75 and >75 years). The two-sided probability values were calculated. $P < 0.05$ was considered to indicate a statistically significant difference. All statistical analyses were performed using SPSS (version 24.0; IBM Corp.).

Results

Baseline characteristics. A total of 2,018 eligible patients with duodenal adenocarcinoma diagnosed between 2004 and 2015 were identified in the SEER database. Table I shows the baseline characteristics of the patients stratified by marital status. Of the 2,018 patients, 1,227 (60.80%) were married and 791 (39.20%) were unmarried, with median ages of 67 and 69 years, respectively. The married group was comprised of considerably more males than females (63.33 vs. 36.67%), whereas the opposite was true in the unmarried group (37.04 vs. 62.96%). There were large proportions of white patients in the married and unmarried groups (79.38 and 66.62%, respectively), and also large proportions of patients who had received surgical interventions (64.38 and 56.89, respectively). There were statistically significant intergroup differences with regard to age ($P < 0.001$), sex ($P < 0.001$), ethnicity ($P < 0.001$), AJCC TNM stage ($P < 0.001$) and surgical details ($P = 0.001$).

Marital status and OS. Survival differed according to marital status ($P < 0.001$), as shown by the Kaplan-Meier curve for OS in Fig. 1A. OS time was higher in married patients compared with that in unmarried patients, with median values of 22 and 12 months, respectively. Similarly, the 5-year OS rate was higher in married patients compared with that in unmarried patients (32.6 vs. 26.8%). In univariate analysis, all variables were identified as significantly predictive factors for OS, aside from ethnicity. After adjustment in multivariate analysis, all aforementioned variables retained independent significance in OS, except for year of diagnosis between 2007 and 2009 ($P = 0.562$), while African descent ($P = 0.387$) or other ethnicity ($P = 0.296$) variables remained non-significant. Unmarried status had a validated negative effect on survival outcomes compared with married status [hazard ratio (HR), 1.259; 95% CI, 1.118-1.419; $P < 0.001$] (Table II).

Table I. Baseline demographic and tumor characteristics of patients in the Surveillance, Epidemiology and End Results database.

Characteristic	Total	Married, n (%)	Unmarried, n (%)	P-value
Patients, n (%)	2,018 (100.00)	1,227 (60.80)	791 (39.20)	
Median age (25th-75th percentile), years	68 (58-76)	67 (57-75)	69 (59-79)	<0.001
Year of diagnosis, n (%)				0.053
2004-2006	409 (20.27)	262 (21.35)	147 (18.58)	
2007-2009	466 (23.09)	261 (21.27)	205 (25.92)	
2010-2012	556 (27.55)	351 (28.61)	205 (25.92)	
2013-2015	587 (29.09)	353 (28.77)	234 (29.58)	
Sex, n (%)				<0.001
Female	948 (46.98)	450 (36.67)	498 (62.96)	
Male	1,070 (53.02)	777 (63.33)	293 (37.04)	
Ethnicity, n (%)				<0.001
Caucasian	1,501 (74.38)	974 (79.38)	527 (66.62)	
African descent	358 (17.74)	156 (12.71)	202 (25.54)	
Other	159 (7.88)	97 (7.91)	62 (7.83)	
Grade, n (%)				0.357
I	376 (18.63)	216 (17.60)	160 (20.23)	
II	908 (45.00)	569 (46.37)	339 (42.86)	
III	705 (34.94)	425 (34.64)	280 (35.40)	
IV	29 (1.44)	17 (1.39)	12 (1.52)	
AJCC TNM stage, n (%)				<0.001
I	406 (20.12)	217 (17.69)	189 (23.89)	
II	387 (19.18)	248 (20.21)	139 (17.57)	
III	609 (30.18)	406 (33.09)	203 (25.66)	
IV	616 (30.53)	356 (29.01)	260 (32.87)	
Surgery, n (%)				<0.001
Yes	1,240 (61.45)	790 (64.38)	450 (56.89)	
No	778 (38.55)	437 (35.62)	341 (43.11)	

AJCC, American Joint Committee on Cancer; TNM, Tumor-Node-Metastasis.

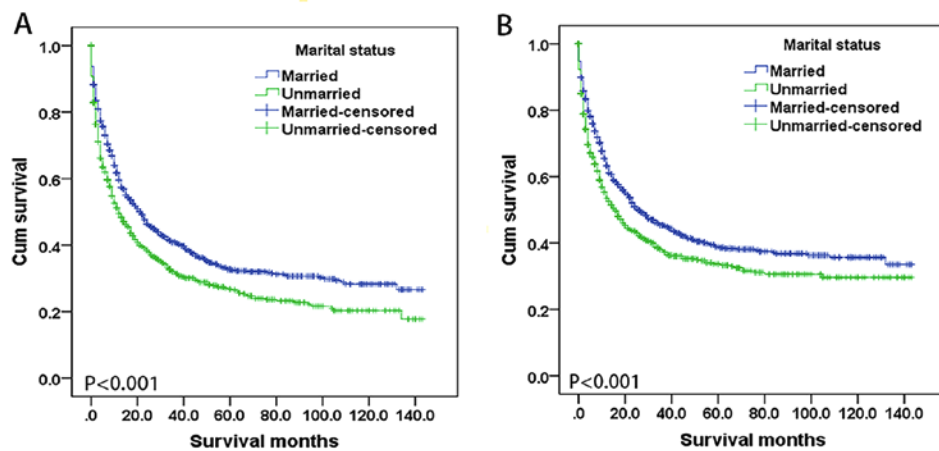


Figure 1. Survival curves in patients with duodenal adenocarcinoma comparing married and unmarried patients. (A) Overall survival. (B) Cause-specific survival. Cum, cumulative.

Marital status and CSS. Representative Kaplan-Meier curves for CSS are presented in Fig. 1B. The 5-year CSS rate was higher for married patients compared with unmarried patients (38.8

vs. 33.7%) and a log-rank test indicated that the difference was significant ($P < 0.001$). In univariate analysis, all variables were identified as significantly predictive factors for CSS, aside from

Table II. Univariate and multivariate survival analysis of OS in patients with duodenal adenocarcinoma.

Characteristic	5-year OS, %	Univariate analysis			Multivariate analysis		
		HR	95% CI	P-value	HR	95% CI	P-value
Year of diagnosis							
2004-2006	26.1	Reference			Reference		
2007-2009	25.7	0.948	0.814-1.103	0.488	0.955	0.819-1.115	0.562
2010-2012	34.0	0.770	0.660-0.898	0.001	0.852	0.729-0.995	0.043
2013-2015	N/A	0.772	0.652-0.914	0.003	0.805	0.679-0.955	0.013
Age, years							
≤58	46.0	Reference			Reference		
59-75	31.3	1.519	1.312-1.760	<0.001	1.544	1.330-1.791	<0.001
>75	12.8	2.753	2.358-3.215	<0.001	2.585	2.199-3.039	<0.001
Sex							
Female	33.4	Reference			Reference		
Male	27.6	1.129	1.010-1.261	0.032	1.176	1.047-1.322	0.006
Race							
Caucasian	30.8	Reference			Reference		
African descent	29.7	1.038	0.898-1.199	0.614	1.068	0.920-1.239	0.387
Other	26.0	0.976	0.789-1.206	0.820	0.892	0.721-1.105	0.296
Marital status							
Married	32.6	Reference			Reference		
Unmarried	26.8	1.303	1.165-1.457	<0.001	1.259	1.118-1.419	<0.001
Grade							
I	56.0	Reference			Reference		
II	29.0	2.073	1.723-2.494	<0.001	1.552	1.278-1.884	<0.001
III	19.1	2.963	2.457-3.547	<0.001	2.105	1.722-2.572	<0.001
IV	22.3	2.740	1.731-4.336	<0.001	2.349	1.473-3.745	<0.001
AJCC TNM stage							
I	53.0	Reference			Reference		
II	36.3	1.433	1.171-1.752	<0.001	1.451	1.171-1.798	0.001
III	36.4	1.386	1.153-1.667	0.001	1.722	1.405-2.110	<0.001
IV	6.2	4.375	3.665-5.223	<0.001	2.427	1.994-2.953	<0.001
Surgery							
Yes	46.4	Reference			Reference		
No	3.9	4.610	4.097-5.188	<0.001	3.399	2.914-3.964	<0.001

OS, overall survival; HR, hazard ratio; CI, confidence interval; AJCC, American Joint Committee on Cancer; N/A, not available; TNM, Tumor-Node-Metastasis.

ethnicity and sex. After adjustment in multivariate analysis, all aforementioned variables retained independent significance in CSS, except for year of diagnosis between 2007 and 2009 ($P=0.612$), year of diagnosis between 2010 and 2012 ($P=0.221$), African ethnicity ($P=0.825$) or other ethnicity ($P=0.092$), and male patients ($P=0.071$). Unmarried status had a validated negative effect on survival outcomes compared with married status (HR, 1.236; 95% CI, 1.086-1.407; $P<0.001$; Table III).

Subgroup analysis of the effect of marital status according to sex. The association between marital status and survival was analyzed separately for the two sexes. Fig. 2 shows Kaplan-Meier survival curves according to marital status and

sex. The 5-year OS rate among female patients was higher in the married group (41.0%) compared with the unmarried group (26.6%) ($P<0.001$), as was the 5-year CSS rate (46.3 vs. 33.0%; $P<0.001$). The 5-year OS rate was also higher for the married group (27.8%) compared with the unmarried group (27.0%) ($P=0.031$) in male patients, whereas their CSS rate did not differ significantly with marital status ($P=0.212$). Multivariate analysis indicated that marital status affects OS in both females (HR, 1.220; 95% CI, 1.024-1.454; $P=0.026$) and males (HR, 1.273; 95% CI, 1.078-1.503; $P=0.004$), and also CSS in both females (HR, 1.218; 95% CI, 1.009-1.470; $P=0.040$) and males (HR, 1.218; 95% CI, 1.014-1.463; $P=0.035$; Table IV).

Table III. Univariate and multivariate survival analysis of CSS in patients with duodenal adenocarcinoma.

Characteristic	5-year CSS, %	Univariate analysis			Multivariate analysis		
		HR	95% CI	P-value	HR	95% CI	P-value
Year of diagnosis							
2004-2006	32.0	Reference			Reference		
2007-2009	32.9	0.934	0.792-1.103	0.421	0.985	0.810-1.133	0.612
2010-2012	40.1	0.790	0.669-0.932	0.005	0.901	0.762-1.065	0.221
2013-2015	N/A	0.766	0.639-0.919	0.004	0.823	0.685-0.989	0.038
Age, years							
≤58	49.7	Reference			Reference		
59-75	38.1	1.377	1.179-1.609	<0.001	1.390	1.187-1.627	<0.001
>75	20.2	2.478	2.102-2.921	<0.001	2.325	1.958-2.760	<0.001
Sex							
Female	39.4	Reference			Reference		
Male	34.5	0.102	0.978-1.242	0.111	1.123	0.990-1.274	0.071
Race							
Caucasian	36.5	Reference			Reference		
African descent	37.5	0.969	0.827-1.136	0.697	0.982	0.833-1.156	0.825
Other	38.9	0.885	0.698-1.121	0.310	0.815	0.642-1.034	0.092
Marital status							
Married	38.8	Reference			Reference		
Unmarried	33.7	1.273	1.128-1.436	<0.001	1.236	1.086-1.407	<0.001
Grade							
I	69.5	Reference			Reference		
II	35.0	2.690	2.153-3.362	<0.001	1.919	1.523-2.419	<0.001
III	22.9	4.071	3.254-5.093	<0.001	2.717	2.145-3.441	<0.001
IV	23.3	3.923	2.418-6.365	<0.001	3.237	1.979-5.294	<0.001
AJCC TNM stage							
I	67.3	Reference			Reference		
II	44.8	1.762	1.390-2.234	<0.001	1.666	1.298-2.140	<0.001
III	42.2	1.786	1.435-2.222	<0.001	2.116	1.668-2.685	<0.001
IV	7.3	6.143	4.984-7.571	<0.001	3.057	2.435-3.838	<0.001
Surgery							
Yes	54.6	Reference			Reference		
No	5.9	5.163	4.544-5.866	<0.001	3.746	3.165-4.434	<0.001

CSS, cause-specific survival; HR, hazard ratio; CI, confidence interval; AJCC, American Joint Committee on Cancer; N/A, not available; TNM, Tumor-Node-Metastasis.

Subgroup analysis of the effect of marital status according to AJCC TNM stage. Fig. 3 shows Kaplan-Meier survival curves according to marital status of the patients at the four AJCC TNM stages: I, n=406; II, n=387; III, n=609; and IV, n=616. For stage-I patients, both the 5-year OS (P<0.001) and CSS (P=0.001) rates were significantly higher in the married group (61.5 and 74.6%, respectively) compared with the unmarried group (43.2 and 58.4%, respectively). In addition, for stage-IV patients, the 5-year OS rates (6.5 vs. 5.8%; P=0.008) and 5-year CSS rates (7.7 vs. 6.9%; P=0.008) were similarly higher in the married group compared with the unmarried group, while the survival rates did not differ significantly with marital status for either AJCC TNM stage II or III. Multivariate analysis showed

that married status was an independent prognostic factor for OS (HR, 1.778; 95% CI, 1.286-2.459; P<0.001) and CSS (HR, 1.732; 95% CI, 1.162-2.583; P=0.007) in patients at stage I, but not in those at stage II, III, or IV (Table V).

Discussion

The present study used the SEER database to investigate the association between marital status and survival outcomes in patients with duodenal adenocarcinoma. OS and CSS rates were higher in married patients compared with those in unmarried patients in both the univariate and multivariate analyses. Marital status may therefore be an independent prognostic

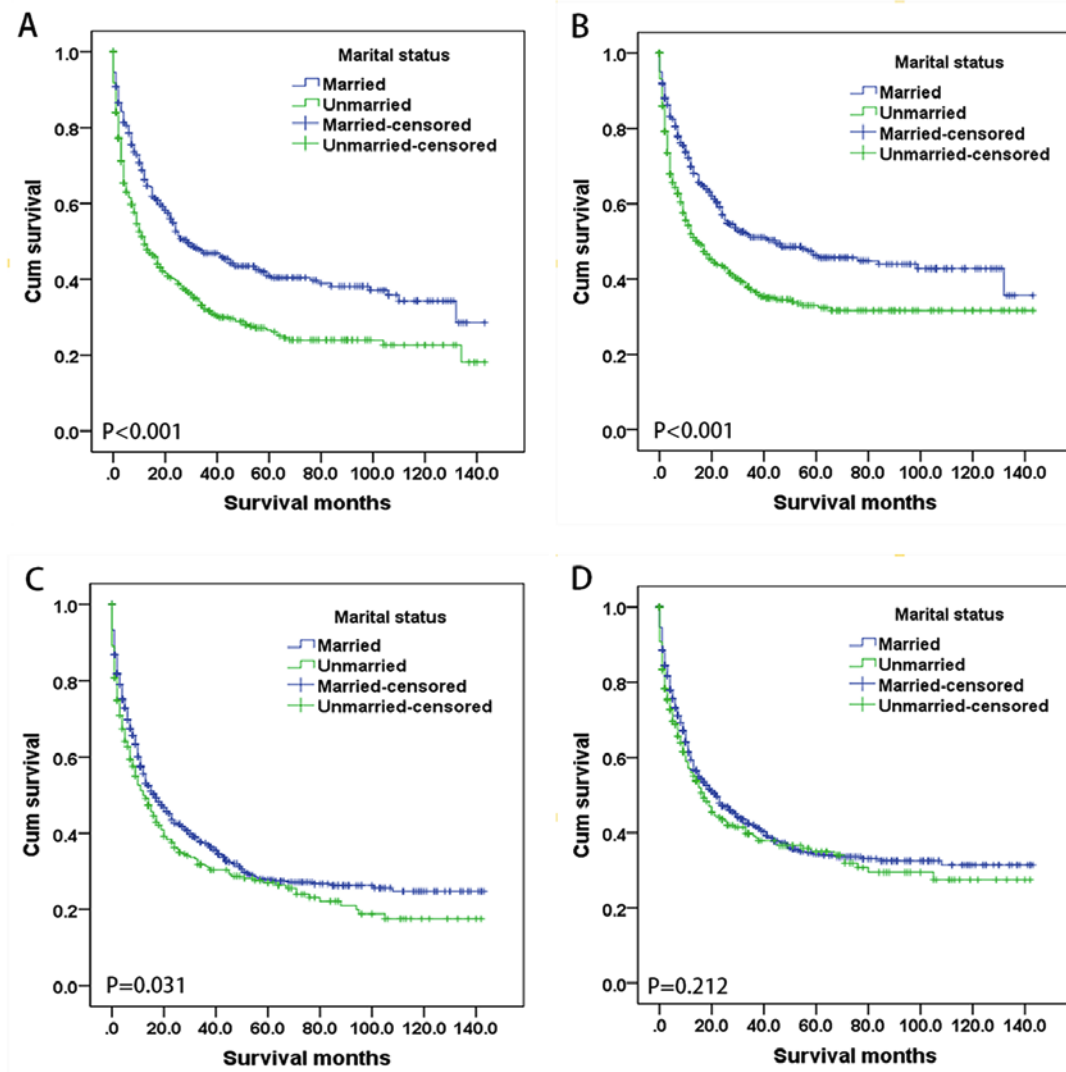


Figure 2. Survival curves in the different sex subgroups of patients with duodenal adenocarcinoma according to marital status. (A) Female OS. (B) Female CSS (C) Male OS. (D) Male CSS. OS, overall survival; CSS, cause-specific survival; Cum, cumulative.

factor for survival in patients with duodenal adenocarcinoma. The results of the present study are consistent with previous studies showing that both OS and CSS rates are increased in patients who are married compared with unmarried patients (including separated/divorced, widowed and unmarried patients) (14,20-25).

In the present study, there was a larger proportion of male patients who were married compared with female patients, and this may be associated with differences in duodenal adenocarcinoma development in the sexes. Generally, there were more male patients than female patients with duodenal adenocarcinoma, consistent with the result that there were more married male participants compared with female participants (26). Additionally, ethnic differences and the financial and social responsibilities associated with marriage may provide an explanation for the differences observed. Socially, Caucasian men are more likely to have a higher education and income when compared with men of other ethnicities, therefore, the marriage rate may be higher (27). A previous study has indicated that the impact of marital status on the survival outcomes for certain types of cancer

differs between men and women (28). Therefore, the present cohort was stratified according to sex in order to analyze whether the effect of marital status on the survival of patients with duodenal adenocarcinoma differed between the sexes, and it was found that both OS [females (HR, 1.220; 95% CI, 1.024-1.454; $P=0.026$) and males (HR, 1.273; 95% CI, 1.078-1.503; $P=0.004$)] and CSS [females (HR, 1.218; 95% CI, 1.009-1.470; $P=0.040$) and males (HR, 1.218; 95% CI, 1.014-1.463; $P=0.035$)] were increased in married patients compared with those in unmarried patients in each sex. The results of the subgroup analyses were similar to those found by Zhou *et al* (19).

Previous studies have suggested that the prognosis may be worse in unmarried patients due to a delayed diagnosis at more advanced tumor stages in such patients (16,29). However, the present subgroup analysis of AJCC TNM stages showed that marital status is only an independent prognostic factor for OS and CSS in patients with stage-I disease, but not in those with disease at stage II, III or IV. Therefore, marital status was a protective factor for patients with early-stage disease, and its impact should not be ignored.

Table IV. Univariate and multivariate survival analysis of patients with duodenal adenocarcinoma based on sex.

A, OS							
Characteristic	5-year survival, %	Median survival time, months	Univariate analysis		Multivariate analysis		
			Log rank χ^2	P-value	HR	95% CI	P-value
Female			28.356	<0.001			
Married	41.0	29			Reference		
Unmarried	26.6	12			1.220	1.024-1.454	0.026
Male			4.648	0.031			
Married	27.8	17			Reference		
Unmarried	27.0	12			1.273	1.078-1.503	0.004

B, CSS							
Characteristic	5-year survival, %	Median survival time, months	Univariate analysis		Multivariate analysis		
			Log rank χ^2	P-value	HR	95% CI	P-value
Female			24.144	<0.001			
Married	46.3	45			Reference		
Unmarried	33.0	15			1.218	1.009-1.470	0.040
Male			1.558	0.212			
Married	34.3	22			Reference		
Unmarried	35.0	17			1.218	1.014-1.463	0.035

OS, overall survival; CSS, cause-specific survival; HR, hazard ratio; CI, confidence interval.

The generally accepted explanations as to why the survival rate of cancer is higher in married patients compared with that in unmarried patients involve improved mental health and socio-economic status (30). It has been proposed that psychology, living habits and economic conditions, as well as certain biological factors, are all strongly associated with marriage and lead to different degrees of physiological changes (31,32). From the physiological viewpoint, there have been numerous reasonable explanations for the mechanism underlying the impact of psychosocial factors on cancer survival rates. The positive effect of marital status on the cancer-related death rate is usually attributable to social support behaviors, including the spouse encouraging healthy behaviors, seeking curative treatment for the patient, and helping to reduce anxiety and stress both during and after treatment (13,33). The socioeconomic status is generally higher for married patients compared with that for unmarried individuals. High medical expenses associated with receiving care usually put the patient under greater financial pressure, and a family member with another source of income may significantly ameliorate this situation (34,35); this is particularly applicable in non-European countries, where the financial resources of patients have greater effects on their access to health care. Without sufficient funds to pay for treatment, some unmarried patients may be unwilling to seek the care they need in a timely manner (36).

In comparing the two groups of patients in this study, it can be seen that unmarried and married patients are comparable

with regard to disease progression at the time of diagnosis, that is, there were no significant differences in pathological grades between the two groups. However, when analyzing the ratio of surgical treatment, unmarried patients did not undergo such treatment modalities as frequently as their married counterparts, and this translates into poor survival for widowed patients whose death risk increased by 101.4% and 5-year CSS was 59.8% compared to married patients (76.1%) (13). Therefore, although unmarried and married patients may present with similar disease processes, they differ in subsequent treatment options, with married patients being more likely to receive active treatment. In addition, there are reports that for unmarried individuals, compliance with clinical appointments is poor (37).

Previous studies have shown that a lack of psychosocial support and increased psychological stress can affect the normal functioning of the immune system, which may promote tumor progression and mortality (38,39). Moreover, inadequate social support can reportedly reduce the activity of natural-killer cells and lead to disorders of various endocrine hormones such as cortisol and catecholamines (35-40). Other studies have shown that cortisol and catecholamines can accelerate the growth and metastasis of malignant tumors via immunosuppression (41-43). In addition, psychological stress can elicit prolonged release of cortisol and lead to cytokine-mediated inflammation, which is considered to be a poor prognostic factor for patients with cancer (44,45). Although the majority of the

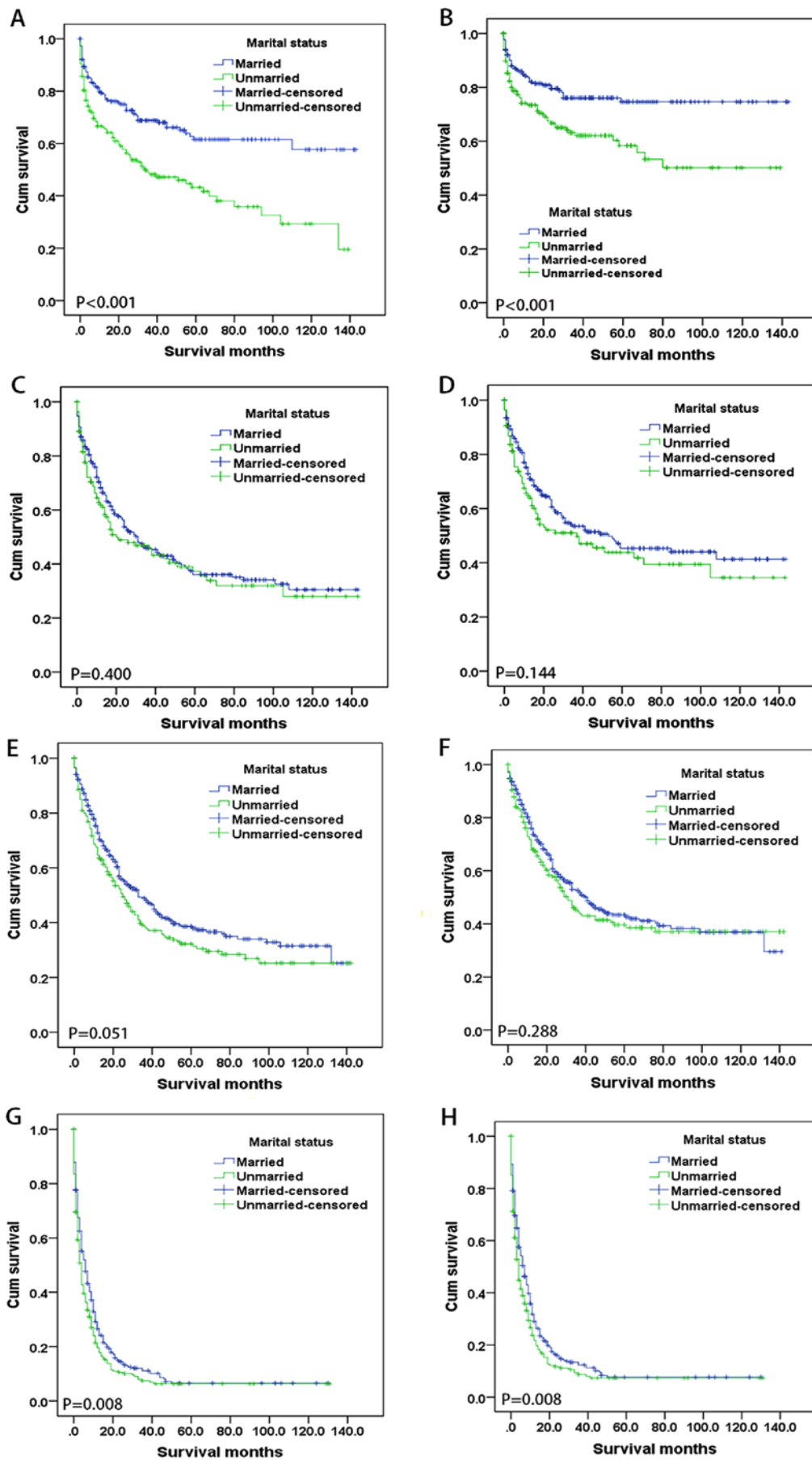


Figure 3. Survival curves in different Tumor-Node-Metastasis stage subgroup patients with duodenal adenocarcinoma according to marital status. (A) Stage I OS. (B) Stage I CSS. (C) Stage II OS. (D) Stage II CSS. (E) Stage III OS. (F) Stage III CSS. (G) Stage IV OS. (H) Stage IV CSS. OS, overall survival; CSS, cause-specific survival; Cum, cumulative.

Table V. Univariate and multivariate survival analysis of patients with duodenal adenocarcinoma based on the American Joint Committee on Cancer Tumor-Node-Metastasis stage.

A, OS							
Characteristic	5-year survival, %	Median survival time, months	Univariate analysis		Multivariate analysis		
			Log rank χ^2	P-value	HR	95% CI	P-value
Stage I			19.027	<0.001			
Married	61.5	N/A			Reference		
Unmarried	43.2	34			1.778	1.286-2.459	<0.001
Stage II			0.707	0.400			
Married	36.0	31			Reference		
Unmarried	37.2	20			1.101	0.825-1.468	0.513
Stage III			3.800	0.051			
Married	38.6	33			Reference		
Unmarried	32.2	25			1.226	0.971-1.547	0.087
Stage IV			7.020	0.008			
Married	6.5	6			Reference		
Unmarried	5.8	4			1.176	0.972-1.423	0.096
B, CSS							
Characteristic	5-year survival, %	Median survival time, months	Univariate analysis		Multivariate analysis		
			Log rank χ^2	P-value	HR	95% CI	P-value
Stage I			10.993	0.001			
Married	74.6	N/A			Reference		
Unmarried	58.4	N/A			1.732	1.162-2.583	0.007
Stage II			2.130	0.144			
Married	45.3	53			Reference		
Unmarried	43.8	37			1.255	0.916-1.721	0.157
Stage III			1.129	0.288			
Married	43.4	41			Reference		
Unmarried	39.6	31			1.119	0.867-1.445	0.387
Stage IV			7.000	0.008			
Married	7.7	7			Reference		
Unmarried	6.9	4			1.189	0.976-1.447	0.085

OS, overall survival; CSS, cause-specific survival; HR, hazard ratio; CI, confidence interval; N/A, not available. NE.Bib.

previous studies involved patients with adenocarcinoma outside the duodenum (14,22,24), the psychosocial and physiological mechanisms underlying the effect of marital status on survival may be similar. Additionally, these previous studies support the presence of links between marriage, social support, and the immune response, and their impact on cancer mortality (30,31).

Some limitations of the present study should be considered: i) The SEER database only provides the marital status at the time of diagnosis, and it was not possible to determine if this had changed after the diagnosis, and any such changes might have influenced the results; ii) patients who were not legally married may still have been in same-sex or heterosexual

partnerships; iii) The SEER database lacks detailed information on the quality of marriage (for example, the degree of trust between husband and wife), and whether divorced or widowed patients are in different family relationships, and both of these aspects may affect the prognosis of patients with duodenal adenocarcinoma; and iv) it was not possible to obtain detailed information about disease recurrence, comorbidities, radio-chemotherapy regimens and surgical procedures from the SEER database. The absence of these covariates may partially bias the observations made in the present study.

In summary, marital status may be an independent prognostic factor for OS and CSS in patients with duodenal

adenocarcinoma. The survival rate of married patients was higher compared with that of unmarried patients, irrespective of sex, and thus, marital status plays an important role as a protective factor in patients with early-stage disease.

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Availability of data and materials

The datasets used and/or analyzed during the present study are available from the author on reasonable request.

Authors' contributions

NW and QB contributed equally to the work. NW, QB and JLY conceived the study and completed the manuscript. NW and JLY analyzed and interpreted the data. XR, JY, QL and HH reviewed, collected and analyzed data. XR and JLY supervised the whole study, revised the manuscript and gave final approval of the version to be published. All authors reviewed, edited and approved the present manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

- Suh CH, Tirumani SH, Shinagare AB, Kim KW, Rosenthal MH, Ramaiya NH and Baheti AD: Diagnosis and management of duodenal adenocarcinomas: A comprehensive review for the radiologist. *Abdom Imaging* 40: 1110-1120, 2015.
- Overman MJ, Hu CY, Kopetz S, Abbruzzese JL, Wolff RA and Chang GJ: A population-based comparison of adenocarcinoma of the large and small intestine: Insights into a rare disease. *Ann Surg Oncol* 19: 1439-1445, 2012.
- Cloyd JM, George E and Visser BC: Duodenal adenocarcinoma: Advances in diagnosis and surgical management. *World J Gastrointest Surg* 8: 212-221, 2016.
- Solaini L, Jamieson NB, Metcalfe M, Abu Hilal M, Soonawalla Z, Davidson BR, McKay C and Koehler HM; UK Duodenal Cancer Study Group: Outcome after surgical resection for duodenal adenocarcinoma in the UK. *Br J Surg* 102: 676-681, 2015.
- Onkendi EO, Boostrom SY, Sarr MG, Farnell MB, Nagorney DM, Donohue JH, Kendrick ML, Reid-Lombardo KM, Harmsen WS and Que FG: 15-year experience with surgical treatment of duodenal carcinoma: A comparison of periampullary and extra-ampullary duodenal carcinomas. *J Gastrointest Surg* 16: 682-691, 2012.
- Cloyd JM, Norton JA, Visser BC and Poultides GA: Does the extent of resection impact survival for duodenal adenocarcinoma? Analysis of 1,611 cases. *Ann Surg Oncol* 22: 573-580, 2015.
- Delcore R, Thomas JH, Forster J and Hermreck AS: Improving resectability and survival in patients with primary duodenal carcinoma. *Am J Surg* 166: 626-631, 1993.
- Struck A, Howard T, Chiorean EG, Clarke JM, Riffenburgh R and Cardenas HR: Non-ampullary duodenal adenocarcinoma: Factors important for relapse and survival. *J Surg Oncol* 100: 144-148, 2009.
- Han SL, Cheng J, Zhou HZ, Zeng QQ and Lan SH: The surgical treatment and outcome for primary duodenal adenocarcinoma. *J Gastrointest Cancer* 41: 243-247, 2010.
- Ryder NM, Ko CY, Hines OJ, Gloor B and Reber HA: Primary duodenal adenocarcinoma: A 40-year experience. *Arch Surg* 135: 1070-1075, 2000.
- Aizer AA, Chen MH, McCarthy EP, Mendu ML, Koo S, Wilhite TJ, Graham PL, Choueiri TK, Hoffman KE, Martin NE, *et al*: Marital status and survival in patients with cancer. *J Clin Oncol* 31: 3869-3876, 2013.
- Adler RH: Engel's biopsychosocial model is still relevant today. *J Psychosom Res* 67: 607-611, 2009.
- Wu SG, Zhang QH, Zhang WW, Sun JY, Lin Q and He ZY: The effect of marital status on nasopharyngeal carcinoma survival: A Surveillance, Epidemiology and End Results study. *J Cancer* 9: 1870-1876, 2018.
- Wang L, Wilson SE, Stewart DB and Hollenbeck CS: Marital status and colon cancer outcomes in US Surveillance, Epidemiology and End Results registries: Does marriage affect cancer survival by gender and stage? *Cancer Epidemiol* 35: 417-422, 2011.
- Mahdi H, Kumar S, Munkarah AR, Abdalamin M, Doherty M and Swensen R: Prognostic impact of marital status on survival of women with epithelial ovarian cancer. *Psychooncology* 22: 83-88, 2013.
- Osborne C, Ostir GV, Du X, Peek MK and Goodwin JS: The influence of marital status on the stage at diagnosis, treatment, and survival of older women with breast cancer. *Breast Cancer Res Treat* 93: 41-47, 2005.
- Xu C, Liu X, Chen YP, Mao YP, Guo R, Zhou GQ, Tang LL, Lin AH, Sun Y and Ma J: Impact of marital status at diagnosis on survival and its change over time between 1973 and 2012 in patients with nasopharyngeal carcinoma: A propensity score-matched analysis. *Cancer Med* 6: 3040-3051, 2017.
- Wilhelm A, Galata C, Beutner U, Schmied BM, Warschkow R, Steffen T, Brunner W, Post S and Marti L: Duodenal localization is a negative predictor of survival after small bowel adenocarcinoma resection: A population-based, propensity score-matched analysis. *J Surg Oncol* 117: 397-408, 2018.
- Zhou H, Zhang Y, Song Y, Tan W, Qiu Z, Li S, Chen Q and Gao S: Marital status is an independent prognostic factor for pancreatic neuroendocrine tumors patients: An analysis of the Surveillance, Epidemiology, and End Results (SEER) database. *Clin Res Hepatol Gastroenterol* 41: 476-486, 2017.
- Jatoi A, Novotny P, Cassivi S, Clark MM, Midthun D, Patten CA, Sloan J and Yang P: Does marital status impact survival and quality of life in patients with non-small cell lung cancer? Observations from the mayo clinic lung cancer cohort. *Oncologist* 12: 1456-1463, 2007.
- Denberg TD, Beatty BL, Kim FJ and Steiner JF: Marriage and ethnicity predict treatment in localized prostate carcinoma. *Cancer* 103: 1819-1825, 2005.
- Zhang W, Wang X, Huang R, Jin K, Zhangyuan G, Yu W, Yin Y, Wang H, Xu Z and Sun B: Prognostic value of marital status on stage at diagnosis in hepatocellular carcinoma. *Sci Rep* 7: 41695, 2017.
- Nelles JL, Joseph SA and Konety BR: The impact of marriage on bladder cancer mortality. *Urol Oncol* 27: 263-267, 2009.
- Li X, Liu Y, Wang Y, Ruan C, Wang H, Liang X, Sun Y and Hu Z: The influence of marital status on survival of gallbladder cancer patients: A population-based study. *Sci Rep* 7: 5322, 2017.
- Zhang J, Gan L, Wu Z, Yan S, Liu X and Guo W: The influence of marital status on the stage at diagnosis, treatment, and survival of adult patients with gastric cancer: A population-based study. *Oncotarget* 8: 22385-22405, 2017.
- Kakushima N, Ono H, Yoshida M, Takizawa K, Tanaka M, Kawata N, Ito S, Imai K, Hotta K, Ishiwatari H and Matsubayashi H: Characteristics and risk factors for sporadic non-ampullary duodenal adenocarcinoma. *Scand J Gastroenterol* 52: 1253-1257, 2017.

27. Griffith DM, Gunter K and Allen JO: Male gender role strain as a barrier to African American men's physical activity. *Health Educ Behav* 38: 482-491, 2011.
28. Kaplan RM and Kronick RG: Marital status and longevity in the United States population. *J Epidemiol Community Health* 60: 760-765, 2006.
29. Nayeri K, Pitaro G and Feldman JG: Marital status and stage at diagnosis in cancer. *N Y State J Med* 92: 8-11, 1992.
30. Shi RL, Qu N, Lu ZW, Liao T, Gao Y and Ji QH: The impact of marital status at diagnosis on cancer survival in patients with differentiated thyroid cancer. *Cancer Med* 5: 2145-2154, 2016.
31. Aarstad AK, Aarstad HJ and Olofsson J: Quality of life, drinking to cope, alcohol consumption and smoking in successfully treated HNSCC patients. *Acta Otolaryngol* 127: 1091-1098, 2007.
32. Cheungpasitporn W, Thongprayoon C, Srivali N, Vijayvargiya P, Andersen CA, Kittanamongkolchai W, Sathick IJ, Caples SM and Erickson SB: The effects of napping on the risk of hypertension: A systematic review and meta-analysis. *J Evid Based Med* 9: 205-212, 2016.
33. Pinquart M and Duberstein PR: Associations of social networks with cancer mortality: A meta-analysis. *Crit Rev Oncol Hematol* 75: 122-137, 2010.
34. O'Neill CB, Atoria CL, O'Reilly EM, LaFemina J, Henman MC and Elkin EB: Costs and trends in pancreatic cancer treatment. *Cancer* 118: 5132-5139, 2012.
35. Baker MS, Kessler LG, Urban N and Smucker RC: Estimating the treatment costs of breast and lung cancer. *Med Care* 29: 40-49, 1991.
36. Alamanda VK, Song Y and Holt GE: Effect of marital status on treatment and survival of extremity soft tissue sarcoma. *Ann Oncol* 25: 725-729, 2014.
37. Wheeler E, Prettyman A, Lenhard MJ and Tran K: Adherence to outpatient program postoperative appointments after bariatric surgery. *Surg Obes Relat Dis* 4: 515-520, 2008.
38. Moreno-Smith M, Lutgendorf SK and Sood AK: Impact of stress on cancer metastasis. *Future Oncol* 6: 1863-1881, 2010.
39. Garssen B and Goodkin K: On the role of immunological factors as mediators between psychosocial factors and cancer progression. *Psychiatry Res* 85: 51-61, 1999.
40. Levy SM, Herberman RB, Whiteside T, Sanzo K, Lee J and Kirkwood J: Perceived social support and tumor estrogen/progesterone receptor status as predictors of natural killer cell activity in breast cancer patients. *Psychosom Med* 52: 73-85, 1990.
41. Sephton SE, Lush E, Dedert EA, Floyd AR, Rebholz WN, Dhabhar FS, Spiegel D and Salmon P: Diurnal cortisol rhythm as a predictor of lung cancer survival. *Brain Behav Immun* 30 (Suppl): S163-S170, 2013.
42. Lointier P, Wildrick DM and Boman BM: The effects of steroid hormones on a human colon cancer cell line in vitro. *Anticancer Res* 12: 1327-1330, 1992.
43. McEwen BS, Biron CA, Brunson KW, Bulloch K, Chambers WH, Dhabhar FS, Goldfarb RH, Kitson RP, Miller AH, Spencer RL and Weiss JM: The role of adrenocorticoids as modulators of immune function in health and disease: Neural, endocrine and immune interactions. *Brain Res Brain Res Rev* 23: 79-133, 1997.
44. Miller GE, Cohen S and Ritchey AK: Chronic psychological stress and the regulation of pro-inflammatory cytokines: A glucocorticoid-resistance model. *Health Psychol* 21: 531-541, 2002.
45. Formica V, Luccchetti J, Cunningham D, Smyth EC, Ferroni P, Nardecchia A, Tesaro M, Cereda V, Guadagni F and Roselli M: Systemic inflammation, as measured by the neutrophil/lymphocyte ratio, may have differential prognostic impact before and during treatment with fluorouracil, irinotecan and bevacizumab in metastatic colorectal cancer patients. *Med Oncol* 31: 166, 2014.



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