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Marital Status Is a Prognostic Factor for Cardiovascular Mortality but Not a Prognostic Factor for Cancer Mortality in Siewert Type II Adenocarcinoma of the Esophagogastric Junction

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Abstract

Background: The impact of marital status on the prognosis of patients with Siewert type II adenocarcinoma of the esophagogatric junction (AEG) remained unclear. This study aimed to investigate the associations of marital status with cancer-specific death risk and cardiovascular death risk in Siewert type II AEG patients.

Methods: Data for Siewert type II AEG patients were obtained from the Surveillance, Epidemiology, and End Results database from 2010 to 2015. A 1:1 propensity score matching (PSM) was applied to reduce inter-group bias between the married and unmarried groups. Kaplan-Meier analysis, a competing risk model and the Fine-Gray multivariable regression model were used to identify the prognostic value of marital status.

Results: In total, 1,623 subjects were included. After PSM, according to Fine-Gray multivariable regression analysis, there was no significant difference in the cumulative cancer-specific death rate between the married and the unmarried groups (hazard ratio (HR): 1.160, 95% confidence interval (CI): 0.994 - 1.354, P = 0.060). Patients in unmarried group had a higher cardiovascular death rate than patients in married group (HR: 3.066, 95% CI: 1.372 - 6.850, P = 0.006).

Conclusions: Our study demonstrates that unmarried Siewert type II AEG patients are associated with higher cardiovascular death risk but not cancer-specific death risk compared with married patients.

Keywords: Adenocarcinoma of the esophagogatric junction; SEER; Marital status; Competing risk model; Cardiovascular mortality

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Introduction

Gastric cancer is one of the most commonly diagnosed malignant cancers, with one million new cases and 770,000 related deaths each year worldwide [1]. The prevalence of adenocarcinoma of the esophagogastric junction (AEG) has dramatically increased in the past decades, and the prognosis remains dismal [2, 3]. AEG is defined as the tumor that the epicenter of the tumor is within 5 cm of the esophagogastric junction (EGJ) [4]. According to the Siewert classification, AEG is classified into three subgroups: Siewert type I, Siewert type II and Siewert type III [5]. Siewert types I and III AEGs are characterized by a consistent pathology that closely resembles esophageal cancer and gastric cancer, respectively. The treatment strategy for Siewert type II AEG still remains controversial because it is difficult to define its origin. Siewert type II AEG is defined as the tumor with the epicenter located from 1 cm above to 2 cm below the EGJ, and is usually defined as the true tumor of EGJ. Previous studies have mainly focused on cancer-specific death in Siewert type II AEG patients [6]. However, related research for cardiovascular death (CVD), as the major cause of non-cancer-specific mortalities, is relatively scarce in the worldwide. Therefore, further studies are urgently needed to identify the prognostic factors for CVD in Siewert type II AEG patients.

Previous studies largely focused on the relationship between clinicopathological characteristics, anti-tumor therapy status and cardiovascular mortalities (CVMs) in patients with cancer [7-9]. Several studies reported that socioeconomic factors, especially marital status, are prognostic factors for CVD in patients with cancer [8, 10]. However, the prognostic value of marital status for CVM in patients with Siewert type II AEG is rarely reported. The clinical value of marital status for Siewert type II AEG patients remains unknown. Therefore, more real-world studies are needed to confirm the impact of marital status in Siewert type II AEG patients.

Materials and Methods

Patient cohort

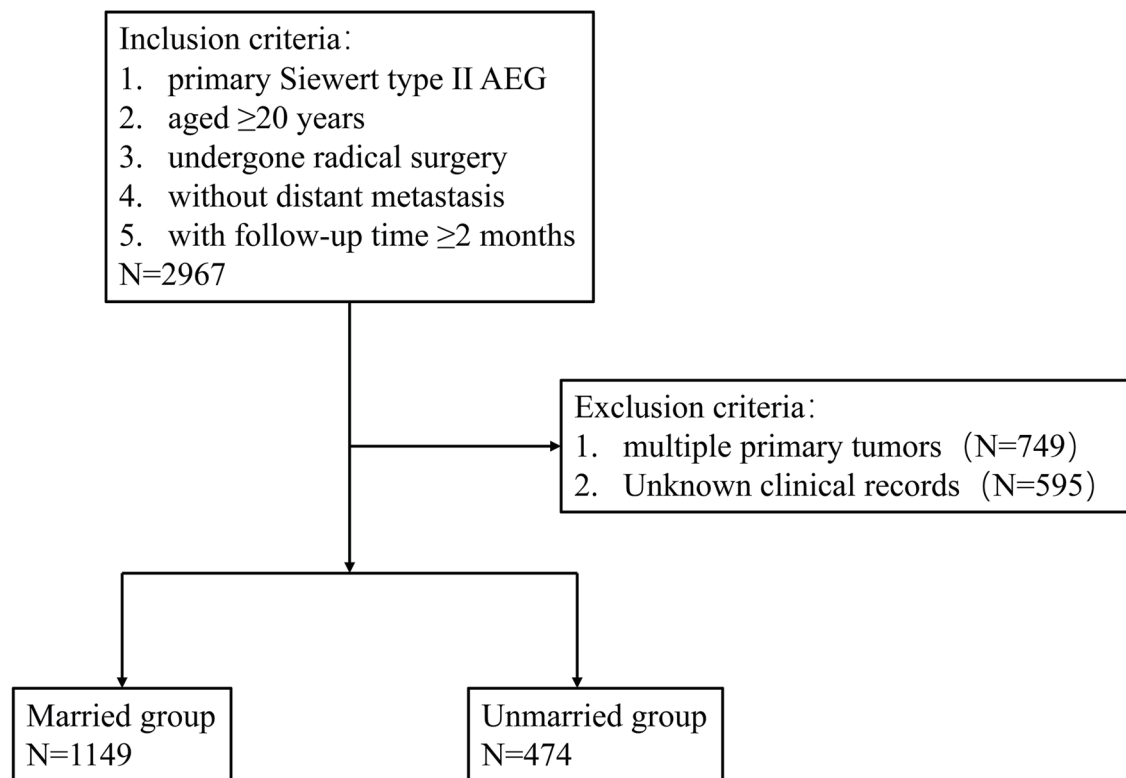The Surveillance, Epidemiology, and End Results (SEER) pro-

Figure 1. Eligibility, inclusion, and exclusion criteria of the study population. AEG: adenocarcinoma of the esophagogatric junction.

gram of the National Cancer Institute (NCI) is a cancer database that consists of clinical data of cancer patients from 18 registries and covers approximately 28% of the United States population [11]. The data of Siewert type II AEG patients with primary resection and regional lymph nodes dissection in the SEER database between January 2010 and December 2015 were extracted from SEER*Stat software version 8.3.9 (Information Management Service, Inc., Calverton, MD, USA). Although the information of Siewert AEG classification was not included in the SEER database, Siewert type II patients satisfied a primary site entry of "Cardia, NOS" and a collaborative staging (CS) Schema V0204+entry of "EsophagusGEJunction" were extracted [12, 13]. All procedures were performed in accordance with guidelines in NCI SEER program [14]. The SEER database is a public anonymized database, so ethical approval was not required for this retrospective study. The inclusion criteria included the following: 1) primary Siewert type II AEG (histology codes based on ICD-O-3: 8140-8147, 8160-8162, 8180-8221, 8250-8507, 8514-8551, 8571-8574, 8576, and 8940-8941); 2) aged ≥ 20 years; 3) undergone radical surgery (surgery encode: 30-80) and regional lymph node dissection; 4) without distant metastasis; 5) with follow-up time ≥ 2 months. Patients with missing or unknown clinical records and with multiple primary tumors were excluded in this study. The selection procedure is shown in Figure 1.

In our study, the following variables were included: age at diagnosis, sex, race, grade, stage, T status according to American Joint Committee on Cancer (AJCC) seventh edition, N status according to AJCC seventh edition, number of removed

lymph nodes (RLN), lymph node metastasis ratio (LNR), tumor size, chemotherapy status, radiotherapy status, marital status, vital status, survival months, and cause of death.

A total of 1,623 Siewert type II AEG patients were included in the study. Patients were categorized into two groups: married and unmarried (which includes single, divorced, separated, and widowed individuals), based on their marital status. X-tile was used to determine optimal cutoff values for age (56 and 75 years), RLN (10 and 16), LNR (4.2 and 16.7) and tumor size (19 and 44 mm) [15]. "No/unknown" radiotherapy records were considered as no radiotherapy. "No/unknown" chemotherapy records were considered as no chemotherapy. CVD was defined as death due to cardiovascular disease as follows according to International Classification of Diseases-Tenth Revision: heart disease (I00-I09, I11, I13, I20-I51), hypertension without heart disease (I10, I12), cerebrovascular disease (I60-I69), atherosclerosis (I70), aortic aneurysm and dissection (I71) and other diseases of arteries, arterioles and capillaries (I72-I78).

The final follow-up was performed in November 2021, and the median follow-up was 37 months (ranging from 2 to 107 months). The follow-up period was defined as the time from the data of first diagnosis with AEG to the date of last follow-up or death.

Statistical analysis

In the present study, we used Kaplan-Meier analysis, a competing risk model and the Fine-Gray multivariable regression mod-

el to identify the prognostic value of marital status in Siewert type II AEG patients based on the SEER database. Additionally, we also used Kaplan-Meier analysis, a competing risk model and the Fine-Gray multivariable regression model to further explore the association between marital status and CVD risk.

The statistical analysis in this study was performed in IBM SPSS 24.0 software or R software (Version 4.1.3). To balance the bias between the married and unmarried subgroups, a 1:1 propensity score matching (PSM) was used to match one married patient with one unmarried patient by variables included in baseline [16]. Descriptive statistics and frequency tables were used to summarize the data. Categorical data were evaluated with the Chi-square test. The Kaplan-Meier survival curve analysis was applied to show the difference in overall survival (OS), AGE-specific survival and cardiovascular-specific survival between the married group and unmarried group, while the log-rank test was performed to estimate differences among groups. Competing risk model analysis and Gray's test were used to identify statistical differences between AGE-specific death and non-AGE-specific death or cardiovascular disease-specific death and non-cardiovascular disease-specific death due to marital status by using the R package cmprsk. The Fine-Gray multivariable regression model was used to examine associations between factors and AEG cancer-specific death or cardiovascular disease-specific death. The difference was considered statistically significant for a two-sided P value < 0.05.

Results

Baseline characteristics

A total of 1,623 patients with Siewert type II AEG were included in this study before PSM. There were significant differences in age (P = 0.025), sex (P < 0.001) and race (P < 0.001) between married and unmarried groups. After PSM, 948 AEG patients were eventually included. There were no statistically differences between the two groups on the mentioned factors, except sex (P = 0.04), race (P < 0.001) and chemotherapy status (P = 0.04). The key information of the variables is shown in Table 1.

Kaplan-Meier survival analysis

OS, cancer-specific survival and cardiovascular disease-specific survival in Siewert type II AEG patients were explored using Kaplan-Meier analysis. Among all 1,623 patients included in this study, 937 (57.73%) died. Compared with patients in the married group, patients in the unmarried group had worse OS, cancer-specific survival and cardiovascular disease-specific survival both before and after PSM (Fig. 2).

Association of marital status with cancer death risk in patients with Siewert type II AEG

In this study, a total of 937 patients died before PSM, of which

84.74% (794/937) were cancer-specific death. According to a competing risk model, there was no significant difference in the cumulative cancer-specific death rate between the married and the unmarried groups (Gray's test, P = 0.08) (Fig. 3). To further investigate the independent prognostic factors of cancer-specific death, the Fine-Gray multivariable regression model was established (Table 2). We noted no statistically significant difference for marital status between groups (hazard ratio (HR): 1.160, 95% confidence interval (CI): 0.994 - 1.354, P = 0.060). Additionally, compared with the corresponding subgroups, patients with age 56 - 75 years, grade G3, higher T status, higher N status, and lower RLN tended to have significantly higher cancer-specific death (P < 0.05).

A total of 565 patients died after PSM, of which 84.07% (475/565) were cancer-specific death. A similar phenomenon was observed. There was still no significant difference in the cumulative cancer-specific death rate between the married and the unmarried groups (Gray's test, P = 0.15) (Fig. 3), and there was no statistically significant difference for marital status between groups (HR: 1.179, 95% CI: 0.975 - 1.426, P = 0.089) (Table 2). Compared with the corresponding subgroups after PSM, patients with grade G3, higher T status, higher N status, lower RLN and larger tumor size tended to have significantly higher cancer-specific death (P < 0.05) (Table 2).

Association of marital status with CVD risk in patients with Siewert type II AEG

To further investigate the association of marital status with CVD risk, a competing risk model and the Fine-Gray multivariable regression were used. As shown in Figure 4, patients in the unmarried group had a higher cumulative cardiovascular disease-specific death rate than patients in married group both before and after PSM. According to the Fine-Gray multivariable regression analysis, unmarried status was related to increased CVD risk before PSM (HR: 1.860, 95% CI: 1.096 - 3.160, P = 0.021), and the adjusted HR further increased after PSM (HR: 3.066, 95% CI: 1.372 - 6.850, P = 0.006) (Table 3).

Discussion

In the present study, based on the analysis of a cohort of 1,623 patients with Siewert type II AEG in the SEER database from January 2010 to December 2015, we investigated the relationship between survival prognosis and marital status for Siewert type II AEG patients who underwent radical surgery. We confirmed that married patients had better OS and cardiovascular disease-specific survival than unmarried patients, and there was no statistically significant difference for cancer-specific survival between two groups, by using Kaplan-Meier survival analysis, a competing risk model, the Fine-Gray multivariable regression and PSM method.

In current study, based on the Fine-Gray multivariable analysis and PSM method, we have shown that histological grade, T stage, RLN, LNR and tumor size could be prognostic factors for Siewert type II AEG patients. The impacts of his-

Table 1. Baseline Clinical Characteristics of Patients With Siewert Type II AEG

Variables	Before PSM, N (%)			After PSM, N (%)		
	Married	Unmarried	P	Married	Unmarried	P
N	1149	474		474	474	
Age			0.025			0.22
≤ 56	296 (25.8%)	148 (31.2%)		135 (28.5%)	148 (31.2%)	
56 - 75	725 (63.1%)	265 (55.9%)		290 (61.2%)	265 (55.9%)	
> 75	128 (11.1%)	61 (12.9%)		49 (10.3%)	61 (12.9%)	
Sex			< 0.001			0.04
Male	981 (85.4%)	347 (73.2%)		375 (79.1%)	347 (73.2%)	
Female	168 (14.6%)	127 (26.8%)		99 (20.9%)	127 (26.8%)	
Race			< 0.001			< 0.001
White	1003 (85.4%)	404 (85.2%)		404 (85.2%)	404 (85.2%)	
Black	41 (3.6%)	39 (8.2%)		12 (2.5%)	39 (8.2%)	
Other	105 (9.1%)	31 (6.5%)		58 (12.2%)	31 (6.5%)	
Grade			0.882			0.462
G1	69 (6.0%)	33 (7.0%)		22 (4.6%)	33 (7.0%)	
G2	436 (37.9%)	177 (37.3%)		178 (37.6%)	177 (37.3%)	
G3	624 (54.3%)	257 (54.2%)		265 (55.9%)	257 (54.2%)	
G4	20 (1.7%)	7 (1.5%)		9 (1.9%)	7 (1.5%)	
Stage			0.088			0.105
I	234 (20.4%)	85 (17.9%)		93 (19.6%)	85 (17.9%)	
II	285 (24.8%)	142 (30.0%)		113 (23.8%)	142 (30.0%)	
III	630 (54.8%)	247 (52.1%)		268 (56.5%)	247 (52.1%)	
T stage			0.232			0.228
T1	229 (19.9%)	95 (20.0%)		83 (17.5%)	95 (20.0%)	
T2	179 (15.6%)	58 (12.2%)		79 (16.7%)	58 (12.2%)	
T3	680 (59.2%)	288 (60.8%)		283 (59.7%)	288 (60.8%)	
T4	61 (5.3%)	33 (7.0%)		29 (6.1%)	33 (7.0%)	
N stage			0.077			0.076
N0	428 (37.2%)	191 (40.3%)		174 (36.7%)	191 (40.3%)	
N1	399 (34.7%)	143 (30.2%)		174 (36.7%)	143 (30.2%)	
N2	205 (17.8%)	76 (16.0%)		80 (16.9%)	76 (16.0%)	
N3	117 (10.2%)	64 (13.5%)		46 (9.7%)	64 (13.5%)	
RLN			0.911			0.799
≤ 10	294 (25.6%)	120 (25.3%)		117 (24.7%)	120 (25.3%)	
10 - 16	308 (26.8%)	132 (27.8%)		125 (26.4%)	132 (27.8%)	
> 16	547 (47.6%)	222 (46.8%)		232 (48.9%)	222 (46.8%)	
LNR			0.118			0.177
≤ 4.2	619 (53.9%)	258 (54.4%)		264 (55.7%)	258 (54.4%)	
4.2 - 16.7	245 (21.3%)	82 (17.3%)		98 (20.7%)	82 (17.3%)	
> 16.7	285 (24.8%)	134 (28.3%)		112 (23.6%)	134 (28.3%)	
Tumor size			0.338			0.966
≤ 19	207 (15.6%)	74 (15.6%)		73 (15.4%)	74 (15.6%)	
19 - 44	522 (45.4%)	211 (44.5%)		215 (45.4%)	211 (44.5%)	

Table 1. Baseline Clinical Characteristics of Patients With Siewert Type II AEG - *(continued)*

Variables	Before PSM, N (%)			After PSM, N (%)		
	Married	**Unmarried**	**P**	**Married**	**Unmarried**	**P**
> 44	420 (36.6%)	189 (39.9%)		186 (39.2%)	189 (39.9%)	
Chemotherapy			0.148			0.042
Yes	840 (73.1%)	329 (69.4%)		358 (75.5%)	329 (69.4%)	
No	309 (26.9%)	145 (30.6%)		116 (24.5%)	145 (30.6%)	
Radiotherapy			0.325			0.064
Yes	677 (58.9%)	266 (56.1%)		295 (62.2%)	266 (56.1%)	
No	472 (41.1%)	208 (43.9%)		179 (37.8%)	208 (43.9%)	
Dead			< 0.001			< 0.001
Alive	516 (44.9%)	170 (35.9%)		213 (44.9%)	170 (35.9%)	
AEG	547 (47.6%)	247 (52.1%)		228 (48.1%)	247 (52.1%)	
Cardiovascular	33 (2.9%)	26 (5.5%)		8 (1.7%)	26 (5.5%)	
Other	53 (4.6%)	31 (6.5%)		25 (5.3%)	31 (6.5%)	

AEG: adenocarcinoma of the esophagogatric junction; LNR: lymph node metastasis ratio; PSM: propensity score matching; RLN: number of removed lymph nodes.

tological grade and tumor size were widely reported to predict the prognosis of AEG [6, 17]. In our study, patients with higher grade and larger tumor size tended to have a worse prognosis, which was consist with previous studies. Zhu et al reported that N stage and RLN are both prognostic factors for Siewert type II AEG [3, 18]. Guo et al demonstrated that RLN and LNR are related to prognosis of Siewert type II AEG patients without radiation therapy, and LNR is also a prediction factor for Siewert type II AEG patients with radiation therapy [6]. They also reported that N stage is not a prognostic factor for Siewert type II AEG patients. The differences between studies could be attribute to different study population, different groupings and different PSM methods. In our study, N stage, RLN and LNR were included in our multivariable regression model, and the results demonstrated that RLN and LNR rather than N stage were related to the prognosis of patients with Siewert type II AEG.

Marital status, one of the social and psychological factors, has been widely reported to be related with the prognosis of patients with cancer [19-21]. The association of marital status with prognosis of patient with Siewert type II AEG was less frequently reported. Wang et al found that unmarried status was a negative prognostic factor for both OS (HR: 1.20, 95% CI: 1.10 - 1.31, P < 0.001) and cancer-specific survival (HR: 1.29, 95% CI: 1.12 - 1.48, P < 0.001) in Siewert type II AEG patients by using Cox regression analyses [22]. In this study, we demonstrated that there was no statistically difference in the cancer-specific death rate between the married and unmarried groups using competing risk regression analyses. The discrepancies between the two studies could be attributed to the fact that the features included in two studies and the analysis methods used in two studies were different. Therefore, additional studies are needed to verify the impact of marital status on cancer-specific death in Siewert type II AEG patients.

CVD, as the leading cause of non-cancer-specific mor-

talities, has become increasingly appreciated in patients with cancer recent years. As the increasing life span and expectancy, CVD increases among the patients with cancer [23, 24]. Previous studies showed that patients with cancer had a higher CVD rate than patients without cancer [25]. Marital status, as a physiological factor, exhibits a strong relationship to cardiovascular disease [26]. However, the effect of marital status in CVD has not previously been reported in patients with Siewert type II AEG. In our study, we found that patients in unmarried group had a higher CVD rate than patients in married group in Siewert type II AEG patients. To the best of our knowledge, this is the first study of the impact of marital status in cardiovascular prognosis of Siewert type II AEG patients. The cardiovascular benefit of marriage may be associated with social and emotional support. Firstly, supervision and mentally encouragement from spouses promote healthy lifestyle changes. Married patients with cancer are more likely to have a healthier lifestyle than unmarried patients [27, 28]. Secondly, spousal support and supervision from spouses may promote early diagnosis and early treatment for cardiovascular disease for patients with cancer [10, 29]. Thirdly, the cancer diagnosis elicited a range of psychological stress levels, including cancer-related distress, depression, and anxiety, which were identified as risk factors that heighten the likelihood of cardiovascular mortality among individuals with cancer [30].

Inevitably, there are also some notable limitations that need to be addressed in this study. Firstly, unregistered confounding factors and selection bias cannot be avoided due to the retrospective study design. Secondly, we cannot rule out the possibility that risk estimates might be influenced by potential confounders, such as family history and other comorbidities. Thirdly, due to the small sample size, we did not explore the impact of different unmarried status such as divorced, separated, widowed in cardiovascular prognosis of patients with Siewert type II AEG. Finally, we were unable to avoid the pos-
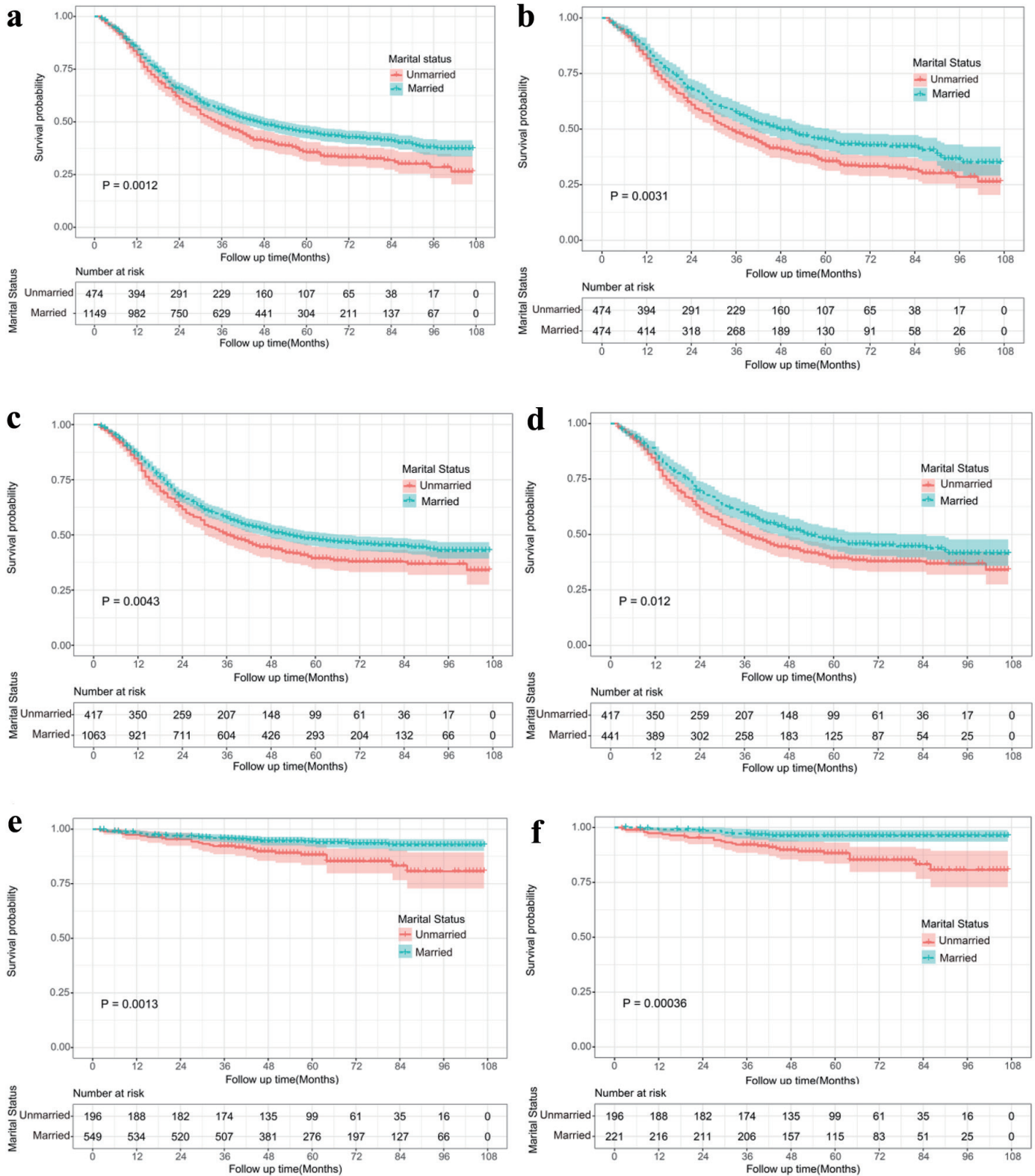
Figure 2. Kaplan-Meier survival analysis for married and unmarried Siewert type II AEG patients. Overall survival curves for the married and unmarried group before (a) and after PSM (b). Cancer-specific survival curves for the married and unmarried group before (c) and after PSM (d). Cardiovascular specific survival curves for the married and unmarried group before (e) and after PSM (f). AEG: adenocarcinoma of the esophagogatric junction; PSM: propensity score matching.
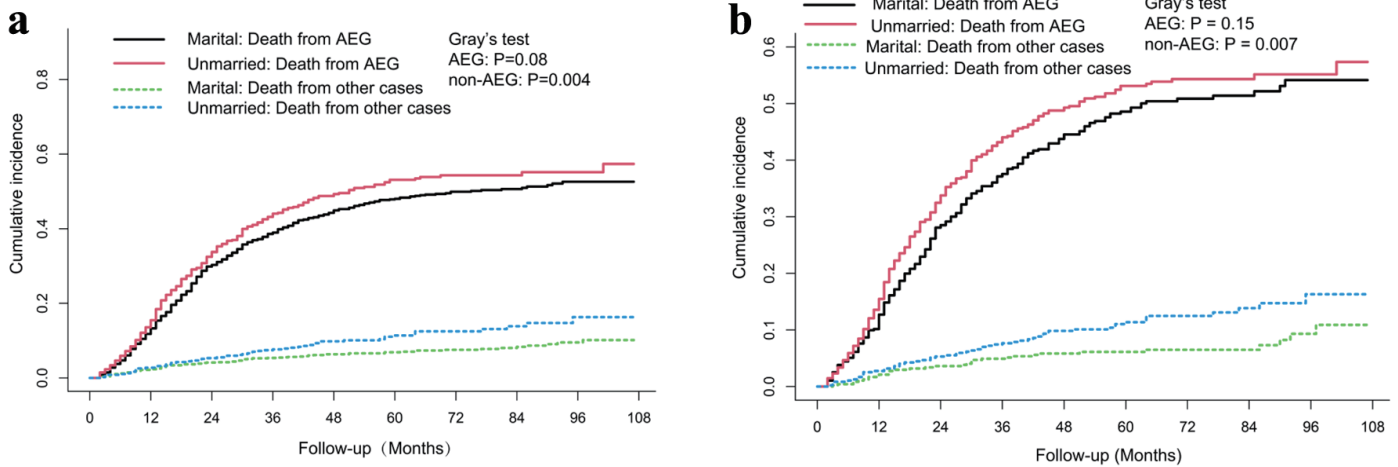
Figure 3. Cumulative incidence of cancer specific death and non-cancer specific death in married and unmarried Siewert type II AEG patients before (a) and after PSM (b). AEG: adenocarcinoma of the esophagogatric junction; PSM: propensity score matching.

Table 2. Multivariable Competing Risk Analysis for Cancer-Specific Death in Patients With Siewert Type II AEG

Variables	Before PSM, N (%)		After PSM, N (%)	
	HR (95% CI)	P	HR (95% CI)	P
Age				
≤ 56	Ref		Ref	
56 - 75	1.176 (1.001 - 1.380)	0.048	1.197 (0.976 - 1.469)	0.084
> 75	1.223 (0.951 - 1.572)	0.12	1.106 (0.795 - 1.539)	0.550
Sex				
Male	Ref		Ref	
Female	0.934 (0.773 - 1.129)	0.48	1.047 (0.839 - 1.307)	0.680
Race				
White	Ref		Ref	
Black	0.930 (0.682 - 1.268)	0.65	0.789 (0.521 - 1.195)	0.260
Other	0.759 (0.576 - 0.999)	0.049	0.797 (0.567 - 1.122)	0.190
Grade				
G1	Ref		Ref	
G2	1.232 (0.848 - 1.790)	0.27	1.588 (0.925 - 2.724)	0.093
G3	1.594 (1.103 - 2.303)	0.013	2.227 (1.311 - 3.785)	0.003
G4	1.575 (0.887 - 2.798)	0.12	1.714 (0.814 - 3.609)	0.160
T stage				
T1	Ref		Ref	
T2	1.745 (1.254 - 2.429)	< 0.001	1.642 (1.070 - 2.521)	0.023
T3	2.053 (1.496 - 2.819)	< 0.001	1.801 (1.199 - 2.705)	0.004
T4	2.808 (1.843 - 4.279)	< 0.001	2.276 (1.346 - 3.848)	0.002
N stage				
N0	Ref		Ref	
N1	1.594 (1.292 - 1.966)	< 0.001	1.500 (1.143 - 1.968)	0.004
N2	2.452 (1.948 - 3.086)	< 0.001	2.517 (1.872 - 3.386)	< 0.001
N3	3.178 (2.453 - 4.117)	< 0.001	2.790 (2.014 - 3.864)	< 0.001

Table 2. Multivariable Competing Risk Analysis for Cancer-Specific Death in Patients With Siewert Type II AEG - *(continued)*

Variables	Before PSM, N (%)		After PSM, N (%)	
	HR (95% CI)	P	HR (95% CI)	P
RLN				
≤ 10	Ref		Ref	
10 - 16	0.774 (0.640 - 0.937)	0.008	0.844 (0.659 - 1.080)	0.180
> 16	0.618 (0.519 - 0.735)	< 0.001	0.634 (0.505 - 0.797)	< 0.001
Tumor size				
≤ 19	Ref		Ref	
19 - 44	1.159 (0.880 - 1.526)	0.30	1.223 (0.844 - 1.770)	0.290
> 44	1.313 (0.983 - 1.752)	0.065	1.700 (1.155 - 2.503)	0.007
Chemotherapy				
Yes	Ref		Ref	
No	1.143 (0.896 - 1.457)	0.28	1.120 (0.826 - 1.518)	0.470
Radiotherapy				
Yes	Ref		Ref	
No	1.046 (0.875 - 1.251)	0.62	1.198 (0.948 - 1.514)	0.130
Marital status				
Married	Ref		Ref	
Unmarried	1.160 (0.994 - 1.354)	0.060	1.179 (0.975 - 1.426)	0.089

AEG: adenocarcinoma of the esophagogatric junction; CI: confidence interval; HR: hazard ratio; RLN: number of removed lymph nodes; PSM: propensity score matching.

sibility that our results might exclude the influence of surgical status because of the focus on surgical cases.

Conclusions

Socioeconomic factors especially marital status were found to be associated with an increased risk of CVM in patients with cancer. However, the clinical value of marital status for Siewert type II AEG patients remains unknown. This study presented a competing risk analysis in a large, population-based, real-world cohort, to further explore the association between marital status and CVD risk. Our study demonstrates that unmarried Siewert type II AEG patients are associated with higher CVD risk but not with cancer-specific death risk compared with married patients. Our results suggest that more attention needs to be offered to unmarried patients with Siewert type II AEG especially for their cardiovascular disease.
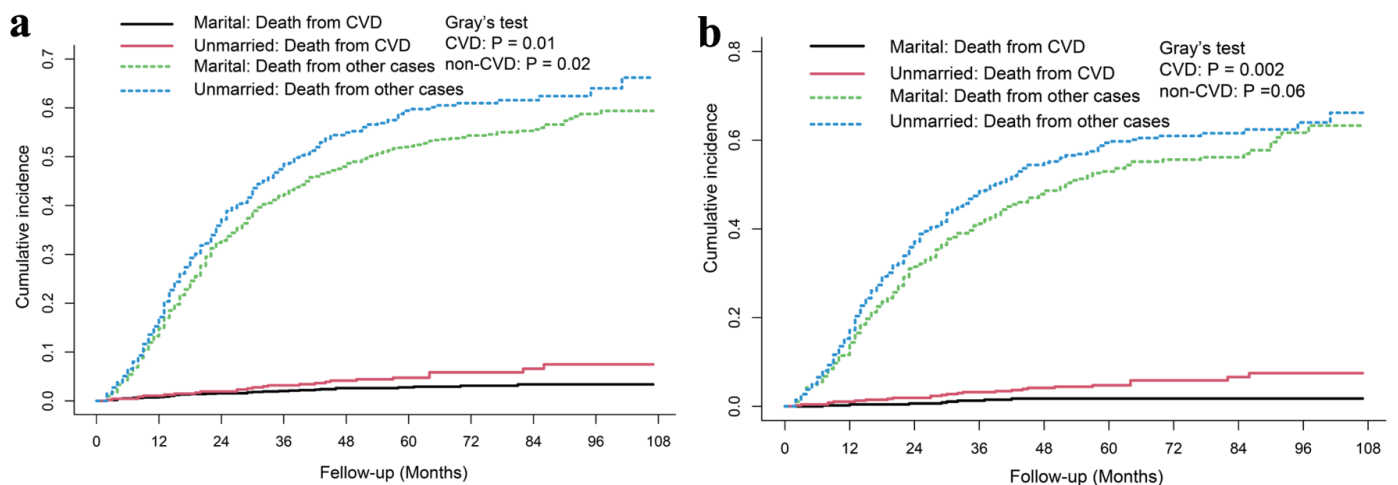

Figure 4. Cumulative incidence of cardiovascular death and non-cardiovascular specific death in married and unmarried Siewert type II AEG patients before (a) and after PSM (b). AEG: adenocarcinoma of the esophagogatric junction; PSM: propensity score matching.

Table 3. Multivariable Competing Risk Analysis for Cardiovascular Death in Patients With Siewert Type II AEG

Variables	Before PSM, N (%)		After PSM, N (%)	
	HR (95% CI)	P	HR (95% CI)	P
Age				
≤ 56	Ref		Ref	
56 - 75	2.149 (0.986 - 4.680)	0.054	1.477 (0.594 - 3.670)	0.400
> 75	3.298 (1.294 - 8.410)	0.012	3.389 (1.124 - 10.220)	0.030
Sex				
Male	Ref		Ref	
Female	0.884 (0.452 - 1.730)	0.720	0.915 (0.408 - 2.050)	0.830
Race				
White	Ref		Ref	
Black	1.983 (0.899 - 4.370)	0.090	3.274 (1.398 - 7.670)	0.006
Other	1.430 (0.616 - 3.320)	0.410	1.412 (0.428 - 4.660)	0.570
Grade				
G1	Ref		Ref	
G2	0.394 (0.139 - 1.110)	0.079	0.702 (0.140 - 3.520)	0.670
G3	0.667 (0.244 - 1.820)	0.430	0.764 (0.153 - 3.820)	0.740
G4	0.645 (0.072 - 5.760)	0.700	1.652 (0.132 - 20.700)	0.700
T stage				
T1	Ref		Ref	
T2	0.817 (0.308 - 2.170)	0.690	0.987 (0.246 - 3.960)	0.990
T3	0.772 (0.338 - 1.770)	0.540	0.927 (0.286 - 3.000)	0.900
T4	0.628 (0.165 - 2.390)	0.490	0.796 (0.151 - 4.200)	0.790
N stage				
N0	Ref		Ref	
N1	1.520 (0.684 - 3.380)	0.300	1.288 (0.448 - 3.700)	0.640
N2	1.209 (0.461 - 3.170)	0.700	2.095 (0.685 - 6.410)	0.190
N3	1.870 (0.773 - 4.530)	0.170	2.310 (0.847 - 6.300)	0.100
RLN				
≤ 10	Ref		Ref	
10 - 16	0.751 (0.370 - 1.530)	0.430	0.628 (0.245 - 1.610)	0.330
> 16	0.850 (0.446 - 1.620)	0.620	0.705 (0.316 - 1.570)	0.390
Tumor size				
≤ 19	Ref		Ref	
19 - 44	2.227 (0.914 - 5.430)	0.078	1.925 (0.556 - 6.670)	0.300
> 44	1.755 (0.677 - 4.550)	0.250	1.207 (0.319 - 4.560)	0.780
Chemotherapy				
Yes	Ref		Ref	
No	1.857 (0.850 - 4.060)	0.120	1.405 (0.423 - 4.670)	0.580
Radiotherapy				
Yes	Ref		Ref	
No	0.865 (0.411 - 1.820)	0.700	0.591 (0.196 - 1.780)	0.350
Marital status				
Married	Ref		Ref	
Unmarried	1.860 (1.096 - 3.160)	0.021	3.066 (1.372 - 6.850)	0.006

AEG: adenocarcinoma of the esophagogatric junction; CI: confidence interval; HR: hazard ratio; PSM: propensity score matching; RLN: number of removed lymph nodes.

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None to declare.

Financial Disclosure

Conflict of Interest

The authors declare no conflict of interest.

Informed Consent

Informed consent was waived.

Author Contributions

ZQZ drafted the manuscript, analyzed data, generated the figure and performed the background research. XZS edited the manuscript. All authors contributed to the article and approved the submitted version.

Data Availability

The data supporting the findings of this study can be obtained in the SEER program.

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