Effect of Marital Status on the Survival of Patients With Adenocarcinoma of the Esophagogastric Junction: A Population-Based, Propensity-Matched Study

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Abstract

Background: Marital status has been reported as an independent prognostic factor in various types of malignancies. However, the association between marital status and outcomes of patients with adenocarcinoma of the esophagogastric junction (AEG) has not been fully explored. To this end, we aimed to investigate the effect of marital status on survival of AEG patients.

Methods: The Surveillance Epidemiology and End Results (SEER) database (2010–2015) was used to extract eligible patients with Siewert type II AEG. Meanwhile, propensity score matching was performed to match 1576 unmarried patients with 1576 married patients. Kaplan–Meier method with log-rank test was used to plot survival curves, univariate and multivariate Cox regression analyses were adopted to investigate the association of marital status with overall survival (OS) and cancer-specific survival (CSS) in AEG patients before and after matching.

Results: Multivariate analysis in the unmatched cohort revealed that marital status was an independent prognostic factor in patients with Siewert type II AEG. Unmarried patients had poorer OS (hazard ratio [HR]: 1.22, 95% confidence interval [CI]: 1.12–1.29, P < .001) and poorer CSS (HR: 1.19, 95% CI: 1.10–1.29, P < .001) than married patients before matching. Additionally, widowed patients had the poorest OS (HR: 1.26, 95% CI: 1.11–1.44, P < .001) and CSS (HR: 1.29, 95% CI: 1.12–1.48, P < .001) compared with married patients. Furthermore, unmarried status remained as an independent prognostic for both OS (HR: 1.20, 95% CI: 1.10–1.31, P < .001) and CSS (HR: 1.18, 95% CI: 1.08–1.30, P < .001) in 1:1 propensity score-matched analysis. Subgroup analysis further revealed that OS and CSS rates were significantly higher in married patients than unmarried ones in most subgroups stratified by different variables.

Conclusions: This population-based study identified that marital status was an independent prognostic indicator for AEG patients. Married AEG patients had better prognosis than their unmarried counterparts.

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Introduction

Adenocarcinoma of the esophagogastric junction (EGJ) is situated at the transition zone between the esophagus and the stomach. The EGJ tumor can be categorized into three subtypes based on the anatomical location according to Siewert: Siewert type I (5 to 1 cm above the EGJ), type II (1 cm above to 2 cm below the EGJ), and type III (2 to 5 cm below the EGJ). Among the three subtypes, Siewert type II is commonly regarded as the true cardia carcinoma, which originates from the esophagogastric junction. The incidence of adenocarcinoma of the esophagogastric junction (AEG) has risen drastically in both Western and Asian countries over the last few decades.

For anti-tumor treatment, surgery remains the primary curative treatment for AEG. Other treatment includes chemotherapy, radiotherapy and newly emerged immune therapy. Neoadjuvant chemoradiotherapy has been reported to improve long-term overall survival (OS) and progression-free survival in patients with esophageal and junctional cancer, followed by surgical resection. Apart from the above therapeutic regimens, endoscopic submucosal dissection (ESD) is a potentially useful, safe, and curative treatment for superficial EGJ cancers. Several studies have reported that en bloc resection rates of ESD for EGJ cancers could reach 90–100%. Despite the continuous advancement in the diagnosis and treatment of AEG, the overall prognosis of AEG patients remains dismal due to high rates of local recurrence and distant metastasis.

Several clinicopathological features have been widely identified to be associated with poor prognosis of patients, including tumor grade, tumor stage at diagnosis, and the performance of surgery or adjuvant therapy. Apart from oncological factors and treatment regimens, psychosocial factors are also associated with the outcome of AEG patients, which have already been demonstrated in several types of cancers. To be specific, previous studies have shown that marital status has significant influence on the outcomes of patients with various types of cancers, including colorectal, gastric, pancreatic, and breast cancers. By analyzing 18 196 patients with gastric cancer selected from Surveillance, Epidemiology, and End Results (SEER) database, a population-based research reported that unmarried patients were at a higher risk of cancer-specific mortality compared with the married group. Additionally, among the unmarried group, widowed patients were at the highest risk of cancer-specific mortality. According to a report by Zhai et al, marriage had a protective effect against cause-specific mortality in breast cancer. However, few studies have examined the impact of marital status on the survival of AEG patients, and the potential association between marital status and AEG survival is still unclear. Thus, we conducted this study to systematically explore the correlation between marital status and survival of AEG patients based on the data provided by SEER cancer registry program.

Methods

Data Sources and Study Population

Our analysis was based on the data obtained from the SEER database. The SEER Program is sponsored by the National Cancer Institute, which assembles and reports data on cancer incidence, treatment, and survival from 18 population-based cancer registries covering approximately 28% of the United States population. We enrolled a total of 11 556 patients diagnosed with Type II AEG between 2010 and 2015 in line with the American Joint Committee on Cancer (AJCC) Cancer Staging Manual (7th edition, 2010). Since the detailed information on the Siewert classification for AEG (type I, II or III) was not directly available in the SEER database, we used the two conditions (‘TNM 7/CS v0204+ Schema’ encoded 28 (EsophagusGEJunction) and “Primary Site – Labelled” encoded 160 (Cardia, NOS)) to specifically identify Siewert type II AEG. The exclusion criteria for the candidates of our study were as follows: (1) patients younger than 18 years old; (2) patients with in situ adenocarcinoma or other type of histology; (3) patients with multiple primary tumors; (4) patients only clinically diagnosed; (5) patients without certain important clinicopathological information, such as AJCC stage, age at diagnosis, race, and marital status; (6) patients with follow-up time less than 6 months; (7) patients without prognostic data. The rest of subjects were enrolled as the eligible cohort of the study. The detailed description of the inclusion/exclusion criteria were shown in Supplemental Figure 1. Since SEER database is publicly available and re-identified, approval was waived by the local ethics committee. Written informed consent was not required in this retrospective study.

Statistical Analysis

Eligible patients were divided into the married group and unmarried group (including divorced/separated, single, and widowed) based on the marital status at diagnosis. Descriptive statistics were performed to investigate the baseline characteristics of patients. Clinicopathological parameters were analyzed and compared by Chi-square (χ²) test. Survival curves were generated by Kaplan–Meier method (both OS and cancer-specific survival (CSS)), and the possible differences were analyzed by log-rank test. Univariate Cox proportional hazard analysis was used to explore possible prognostic...
factors, and variables with $P$ values <.05 were further incorporated into the multivariate Cox proportional hazard model. Results were shown in hazard ratio (HR) and 95% confidence interval (CI).

The major methodological challenges of retrospective studies include systematic differences in baseline covariates and cohort selection bias. Thus, we employed propensity score matching (PSM) to balance baseline covariates between married patients and unmarried patients. Propensity scores (PSs) were calculated using a multivariable logistic regression model to balance two groups (married/unmarried). In this model, marital status was used as the dependent variable and all other recorded variables in Table 1 were used as covariates. We then matched married and unmarried patients who had very similar PSs. Subsequently, 1:1 PS-matching was conducted using the nearest-neighbor algorithm with a caliper

### Table 1. Clinicopathological characteristics of patients before matching.

|                      | Total (N = 4968) | Married (N = 3320) | Unmarried (N = 1648) | $P$ |
|----------------------|------------------|--------------------|----------------------|-----|
| Age                  |                  |                    |                      | .03 |
| ≤65                  | 2691 (54.17)     | 1762 (53.07)       | 929 (56.37)          |     |
| >65                  | 2277 (45.83)     | 1558 (46.93)       | 719 (43.63)          |     |
| Race                 |                  |                    |                      | <.001|
| Black                | 269 (5.41)       | 132 (3.98)         | 137 (8.31)           |     |
| White                | 4341 (87.38)     | 2931 (88.28)       | 1410 (85.56)         |     |
| Other                | 358 (7.21)       | 257 (7.74)         | 101 (6.13)           |     |
| Sex                  |                  |                    |                      | <.001|
| Male                 | 398 (80.25)      | 282 (84.97)        | 1166 (70.75)         |     |
| Female               | 981 (19.75)      | 499 (15.03)        | 482 (29.25)          |     |
| Tumor grade          |                  |                    |                      | .221 |
| Well differentiated   | 280 (5.68)       | 188 (5.66)         | 94 (5.7)             |     |
| Moderately differentiated | 1610 (32.41)  | 1055 (31.78)       | 555 (33.68)          |     |
| Poorly differentiated/undifferentiated | 2396 (48.23) | 1635 (49.25)       | 761 (46.18)          |     |
| Unknown              | 680 (13.69)      | 442 (13.31)        | 238 (14.44)          |     |
| Tumor size (cm)      |                  |                    |                      | .031 |
| ≤2                   | 813 (16.36)      | 557 (16.78)        | 256 (15.53)          |     |
| 2.1–5                | 1683 (33.88)     | 1145 (34.49)       | 538 (32.65)          |     |
| >5                   | 886 (17.83)      | 604 (18.19)        | 282 (17.11)          |     |
| Unknown              | 1586 (31.92)     | 1014 (30.54)       | 572 (34.71)          |     |
| TNM stage            |                  |                    |                      | .057 |
| I                    | 970 (19.52)      | 630 (18.98)        | 340 (20.63)          |     |
| II                   | 932 (18.76)      | 602 (18.13)        | 330 (20.02)          |     |
| III                  | 1635 (32.91)     | 1130 (34.04)       | 505 (30.64)          |     |
| IV                   | 1431 (28.8)      | 958 (28.86)        | 473 (28.7)           |     |
| Surgery              |                  |                    |                      | <.001|
| No                   | 2425 (48.81)     | 1526 (45.96)       | 899 (54.55)          |     |
| Endoscopic resection | 280 (5.64)       | 190 (5.72)         | 90 (5.46)            |     |
| Surgery              | 2249 (45.27)     | 1595 (48.04)       | 654 (39.68)          |     |
| Unknown              | 14 (28)          | 9 (27)             | 5 (3)                |     |
| Radiation            |                  |                    |                      | .752 |
| Yes                  | 2646 (53.26)     | 1774 (53.43)       | 872 (52.91)          |     |
| No/unknown           | 2322 (46.74)     | 1546 (46.57)       | 776 (47.09)          |     |
| Chemotherapy         |                  |                    |                      | <.001|
| Yes                  | 3856 (77.62)     | 2635 (79.37)       | 1221 (74.09)         |     |
| No/unknown           | 1112 (22.38)     | 685 (20.63)        | 427 (25.91)          |     |
| Cause of death       |                  |                    |                      | <.001|
| Alive                | 1855 (37.34)     | 1318 (39.7)        | 537 (32.58)          |     |
| Dead from cancer     | 2794 (56.24)     | 1808 (54.46)       | 986 (59.83)          |     |
| Dead not from cancer | 288 (5.80)       | 175 (5.27)         | 113 (6.86)           |     |
| Unknown              | 31 (62)          | 19 (57)            | 12 (73)              |     |
| Follow-up time (months) median (IQR) | 19 (11, 34) | 20 (12, 35) | 17 (10, 30) | <.001|

Abbreviation: IQR, interquartile range.
width of .1. Standardized mean difference (SMD) was calculated before and after matching and SMD values <.1 indicated that variables were well balanced between 2 groups. After matching, we similarly plotted Kaplan–Meier curves to compare the OS and CSS between married and unmarried patients. Univariate Cox proportional hazard analysis was also performed to identify prognostic factors in the matched cohort.

SPSS version 26.0 (SPSS Inc., Chicago, IL, USA) and R software for Mac version 3.6.1 (The R Foundation for Statistical Computing, Vienna, Austria) were used to analyze data and to plot figures. Results were considered to be statistically significant if a two-sided $P$ value was less than .05.

**Results**

**Characteristics of Patients**

We enrolled 4968 eligible Siewert Type II AEG patients diagnosed from 2010 to 2015 from the SEER database according to the inclusion and exclusion criteria. Patients were further divided into the married group (n = 3320, 66.83%) and unmarried group (n = 1648, 33.17%). The detailed process of screening was shown in Supplemental Figure 1. The baseline clinicopathological features of patients in two groups of marital status were summarized in Table 1. The median age was 64 years old (interquartile range (IQR): 56–72), and the median follow-up time was 19 months (IQR: 11–34). There was a significant difference in age ($P = .03$), race ($P < .001$), sex ($P < .001$), tumor size ($P = .031$), rate of receiving surgery ($P < .001$), and chemotherapy ($P = .001$) between married and unmarried groups. Unmarried AEG patients had higher proportion of younger patients (56.37% vs 53.07%), higher proportion of females (29.25% vs 15.03%), lower rate of surgery (39.68% vs 48.04%), and lower rate of chemotherapy (74.09% vs 79.37%) compared to the married group.

**Prognostic Factors for Patients With AEG Before Matching**

Kaplan–Meier curves were used to evaluate OS and CSS rates of AEG patients. As shown in Figure 1(A) and 1(B), unmarried status was associated with significantly worse

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**Figure 1.** Kaplan–Meier curves of overall survival (OS) and cancer-specific survival (CSS) in AEG patients according to marital status before matching. (A) OS curves between married and unmarried patients. (B) CSS curves between married and unmarried patients. (C) OS curves among married, single, widowed, and divorced/separated patients. (D) CSS curves among married, single, widowed, and divorced/separated patients.
prognosis compared to married status ($P < .0001$). To further explore whether different unmarried status could cause worse prognosis than married status respectively, we partitioned the unmarried group into three subgroups: divorced/separated, single, and widowed patients. As shown in Figure 1(C), compared with married patients, divorced/separated patients, and single patients had significantly decreased OS rates. Widowed patients had the poorest prognosis. Similarly, compared with married patients, divorced patients and single patients also had significantly decreased CSS rates, while widowed patients had the poorest CSS rate (Figure 1(D)).

To investigate possible prognostic factors in AEG patients, we performed univariate and multivariate Cox regression analyses. Variables with $P$ value $< .05$ in the univariate analysis were further incorporated into the multivariate analysis. For marital status, unmarried patients had significantly poorer OS (HR: 1.24, 95% CI: 1.10–1.38, $P < .001$ for divorced/separated patients; HR: 1.18, 95% CI: 1.07–1.31, $P = .001$ for single patients; HR: 1.26, 95% CI: 1.11–1.44, $P < .001$ for widowed patients) and CSS (HR: 1.18, 95% CI: 1.05–1.33, $P = .006$ for divorced/separated patients; HR: 1.15, 95% CI: 1.03–1.27, $P = .010$ for single patients; HR: 1.29, 95% CI: 1.12–1.48, $P < .001$ for widowed patients) than married patients. In addition, multivariate Cox analysis revealed that tumor grade, TNM stage, surgery, and chemotherapy were independent prognostic factors for OS and CSS. And age was significantly associated with OS, but not CSS. The detailed description of each prognostic factor was displayed in Table 2.

**Prognostic Value of Marital Status Stratified by Different Clinicopathological Features Before Matching**

To examine the credibility of our conclusions, we further performed subgroup analysis by dividing patients into the married and unmarried groups. As shown in Figure 2, unmarried status was associated with significantly unfavorable OS and CSS than married status in most subgroups. Although no significance was reached for some subgroup analyses, such as the analyses of patients of black and other races for OS and CSS possibly due to the small sample size, there were trends indicating that unmarried status contributed to poorer OS and CSS in these subgroups.

**Prognostic Significance of Marital Status for Patients With AEG After Matching**

To further verify the finding that married AEG patients had favorable prognosis and to minimize selection bias in this study, PSM analysis was carried out. By using a 1:1 PSM method with a caliper width of .1, we matched 1576 unmarried patients with 1576 married patients. As shown in Table 3, all the baseline variables were well matched (all SMD $< .1$). As shown in Table 4, after PSM analysis, unmarried patients still showed poorer OS (HR: 1.20, 95% CI: 1.10–1.31, $P < .001$) and CSS (HR: 1.18, 95% CI: 1.08–1.30, $P < .001$) in the univariate Cox model. Kaplan–Meier curves were also used to evaluate OS rate and CSS rate of AEG patients with different marital status after matching. As shown in Figure 3(A) and 3(B), unmarried patients still suffered worse prognosis compared to married patients after matching ($P < .001$). Furthermore, compared with married patients, divorced patients and single patients had significantly decreased OS and CSS rates, and widowed patients had the poorest prognosis according to our results after matching (Figure 3(C) and 3(D)). Subgroup analysis was similarly carried out after matching. As shown in Figure 4, most of the subgroup analyses showed that unmarried patients had unfavorable OS and CSS than married patients stratified by different variables. Our results showed the similar effects of marital status on OS and CSS both before and after PSM, further confirming that marital status was an independent prognostic factor for AEG patients.

**Discussion**

This population-based study showed that AEG patients who were unmarried at diagnosis had a significantly higher death risk of all causes compared to the married ones. Moreover, different types of unmarried statuses, including single, widowed, and divorced/separated statuses, all contributed to poorer prognosis than married status. Among the unmarried patients, widowed patients had the poorest prognosis.

Although mounting evidence indicates the adverse effects of unmarried status compared to married status on cancer prognosis,13-15,17,24 the mechanism is not fully understood. The first possible underlying reason why married patients with AEG had better prognosis is that married patients generally have better economic status, which might support them to have easier access to better and earlier medical service and treatment.25-28 Additionally, in this study, we found that married AEG patients were more likely to undergo surgery and endoscopic resection than their counterparts, which indicated that the worse prognosis of unmarried patients can partly be attributed to undertreatment. Similarly, some related researches show that married patients would have better prognosis because they could be diagnosed and undergo treatment at an early stage.29,30 This partly explains why unmarried patients have poorer prognosis than married ones. Another possible reason for the prognostic value of marital status in AEG patients is that married patients could have encouragement and emotional support from their spouses. Unmarried patients lack the support and care from their spouses, thus they often suffer from mental stress, pressure, and even depression. As a result, they are more likely to be indulged in bad habits such as smoking and alcohol abuse, which could cause the development of tumors.31,32 Spouse support plays an important role in helping married patients...
receive medical care and encourage them to have an optimistic attitude towards disease.

Sociopsychological factors, including marital status, can impact the development and prognosis of oncological diseases by regulating the endocrine and immune systems. It has been previously reported that reduced social support and mental stress could activate specific immunosuppression signaling transduction pathways, leading to tumor growth and progression. Levy et al. reported that decreased social support was related with reduced activity of natural killer...
Figure 2. Forest plot summarizing the hazard ratio (HR) for unmarried status vs married status of the (A) overall survival and (B) cancer-specific survival rates of AEG patients in the subgroups according to different clinicopathological factors in the unmatched cohort. The X-axis displays the HR and 95% confidence interval (CI) of each subgroup, ticks are arranged at .5, 1.0, 1.5, 2.0, and 2.5.

Table 3. Clinicopathological Characteristics Between Married and Unmarried Patients Before and After Propensity Score Matching.

| Variable                  | Before Matching | After Matching | SMD | Before Matching | After Matching | SMD |
|---------------------------|-----------------|----------------|-----|-----------------|----------------|-----|
|                           | Married (N = 3320) | Unmarried (N = 1648) | SMD | Married (N = 1576) | Unmarried (N = 1576) | SMD |
| Age                       | .066            | .037           |     | .188            | .049           |     |
| ≤65                       | 1762 (53.07)    | 929 (56.37)    |     | 918 (58.25)     | 889 (56.41)    |     |
| >65                       | 1558 (46.93)    | 719 (43.63)    |     | 658 (41.75)     | 687 (43.59)    |     |
| Race                      | .188            | .049           |     | .348            | .009           |     |
| Black                     | 132 (3.98)      | 137 (8.31)     |     | 105 (6.66)      | 114 (7.23)     |     |
| White                     | 2931 (88.28)    | 1410 (85.56)   |     | 1355 (85.98)    | 1364 (86.55)   |     |
| Other                     | 257 (7.74)      | 101 (6.13)     |     | 116 (7.36)      | 98 (6.22)      |     |
| Sex                       | .489            | .092           |     | .514            | .012           |     |
| Male                      | 2821 (84.97)    | 1166 (70.75)   |     | 1168 (74.11)    | 1162 (73.73)   |     |
| Female                    | 499 (15.03)     | 482 (29.25)    |     | 408 (25.89)     | 414 (26.27)    |     |
| Tumor grade               | .063            | .048           |     | .089            | .028           |     |
| Well differentiated       | 188 (5.66)      | 94 (5.7)       |     | 97 (6.15)       | 88 (5.58)      |     |
| Moderately differentiated | 1055 (31.78)    | 555 (33.68)    |     | 498 (31.6)      | 529 (33.57)    |     |
| Poorly differentiated/undifferentiated | 1635 (49.25) | 761 (46.18) | 760 (48.22) | 735 (46.64) |
| Unknown                   | 442 (13.31)     | 238 (14.44)    |     | 221 (14.02)     | 224 (14.21)    |     |
| Tumor size (cm)           | .089            | .028           |     | .083            | .031           |     |
| ≤2                        | 557 (16.78)     | 256 (15.53)    |     | 255 (16.18)     | 248 (15.74)    |     |
| 2.1–5                     | 1145 (34.49)    | 538 (32.65)    |     | 501 (31.79)     | 521 (33.06)    |     |
| >5                        | 604 (18.19)     | 282 (17.11)    |     | 280 (17.77)     | 274 (17.39)    |     |
| Unknown                   | 1014 (30.54)    | 572 (34.71)    |     | 540 (34.26)     | 533 (33.82)    |     |
| TNM stage                 | .083            | .031           |     | .176            | .034           |     |
| I                         | 630 (18.98)     | 340 (20.63)    |     | 329 (20.88)     | 314 (19.92)    |     |
| II                        | 602 (18.13)     | 330 (20.02)    |     | 298 (18.91)     | 313 (19.86)    |     |
| III                       | 1130 (34.04)    | 505 (30.64)    |     | 495 (31.41)     | 492 (31.22)    |     |
| IV                        | 958 (28.86)     | 473 (28.7)     |     | 454 (28.81)     | 457 (29)       |     |
| Surgery                   | .176            | .034           |     | .83            | .034           |     |
| No                        | 1526 (45.96)    | 899 (54.55)    |     | 830 (52.66)     | 842 (53.43)    |     |
| Endoscopic resection      | 180 (5.72)      | 90 (5.46)      |     | 95 (6.03)       | 88 (5.58)      |     |
| Surgery                   | 1595 (48.04)    | 654 (39.68)    |     | 648 (41.12)     | 641 (40.67)    |     |
| Unknown                   | 9 (.27)         | 5 (.3)         |     | 3 (.19)         | 5 (.32)        |     |

(continued)
Table 3. (continued)

| Variable          | Before Matching | After Matching | SMD | Before Matching | After Matching | SMD |
|-------------------|-----------------|----------------|-----|-----------------|----------------|-----|
|                   | Married (N = 3320) | Unmarried (N = 1648) |     | Married (N = 1576) | Unmarried (N = 1576) |     |
| Radiation         |                 |                 |     |                 |                 |     |
| Yes               | 1774 (53.43)    | 872 (52.91)     |  .010 | 825 (52.35)    | 835 (52.98)     |  .013 |
| No/unknown        | 1546 (46.57)    | 776 (47.09)     |      | 751 (47.65)    | 741 (47.02)     |      |
| Chemotherapy      |                 |                 |     |                 |                 |     |
| Yes               | 2635 (79.37)    | 1221 (74.09)    |  .125 | 1186 (75.25)   | 1188 (75.38)    |  .003 |
| No/unknown        | 685 (20.63)     | 427 (25.91)     |      | 390 (24.75)    | 388 (24.62)     |      |

Abbreviation: SMD, standardized mean difference.

Table 4. Univariate Cox regression model to assess factors associated with overall survival (OS) and cancer-specific survival (CSS) after matching.

|               | OS                  | CSS                |
|---------------|---------------------|--------------------|
|               | HR (95% CI)         | P                  | HR (95% CI)         | P                  |
| Age           |                     |                    |                    |                    |
| ≤65           | Reference           |                    | Reference           |                    |
| >65           | 1.18 (1.08–1.29)    | <.001              | 1.11 (1.01–1.21)    | .035               |
| Race          |                     |                    |                    |                    |
| Black         | Reference           |                    | Reference           |                    |
| White         | .91 (.77–1.08)      | .288               | .92 (.77–1.10)      | .38                |
| Other         | .83 (.66–1.06)      | .133               | .86 (.67–1.11)      | .25                |
| Sex           |                     |                    |                    |                    |
| Male          | Reference           | .007               | Reference           | .005               |
| Female        | .87 (.79–.96)       |                    | .86 (.77–.96)       |                    |
| Marital status|                     |                    |                    |                    |
| Married       | Reference           |                    | Reference           |                    |
| Unmarried     | 1.20 (1.10–1.31)    | <.001              | 1.18 (1.08–1.30)    | <.001              |
| Tumor grade   |                     |                    |                    |                    |
| Well differentiated | Reference        |                    | Reference           |                    |
| Moderately differentiated | 1.74 (1.37–2.20) | <.001              | 2.14 (1.62–2.81)    | <.001              |
| Poorly differentiated/undifferentiated | 2.47 (1.96–3.11) | <.001              | 3.02 (2.32–3.98)    | <.001              |
| Unknown       | 2.03 (1.58–2.61)    | <.001              | 2.39 (1.78–3.19)    | <.001              |
| Tumor size (cm) |                     |                    |                    |                    |
| ≤2            | Reference           |                    | Reference           |                    |
| 2.1–5         | 2.01 (1.72–2.35)    | <.001              | 2.46 (2.05–2.95)    | <.001              |
| >5            | 2.45 (2.06–2.90)    | <.001              | 3.07 (2.53–3.72)    | <.001              |
| unknown       | 2.62 (2.25–3.06)    | <.001              | 3.26 (2.73–3.90)    | <.001              |
| TNM stage     |                     |                    |                    |                    |
| I             | Reference           |                    | Reference           |                    |
| II            | 1.90 (1.62–2.24)    | <.001              | 2.17 (1.80–2.61)    | <.001              |
| III           | 2.33 (2.00–2.70)    | <.001              | 2.90 (2.45–3.44)    | <.001              |
| IV            | 5.36 (4.63–6.21)    | <.001              | 6.99 (5.91–8.26)    | <.001              |
| Surgery       |                     |                    |                    |                    |
| No            | Reference           |                    | Reference           |                    |
| Surgery       | .28 (2.62–31)      | <.001              | .26 (24–29)         | <.001              |
| Endoscopic resection | .15 (12–20)  | <.001              | .09 (06–14)         | <.001              |
| Unknown       | 2.03 (1.01–4.08)    | .046               | 2.42 (1.15–5.09)    | .020               |

(continued)
Social support and reduced stress are associated with the level of cortisol. Cortisol is one of the steroid hormones produced in the adrenal glands, the secretion of cortisol is controlled by the hypothalamus, the pituitary gland, and the adrenal gland (the hypothalamic–pituitary–adrenal (HPA) axis) in response to stress. It has been reported that the HPA axis is activated to suppress T-cell-mediated immune responses in the depressed group.

The influence of sociopsychological factors on the prognosis of cancer patients has gained increasing attention. Positive sociopsychological factors can alleviate the pain and stress of cancer patients, thus increasing their treatment

### Table 4. (continued)

| Radiation     | OS HR (95% CI) | OS P | CSS HR (95% CI) | CSS P |
|---------------|----------------|------|----------------|-------|
| No/unknown    | Reference      | .675 | Reference      | .85   |
| Yes           | 1.02 (.93–1.11)| .675 | 1.01 (.92–1.11)| .85   |
| Chemotherapy  |                |      |                |       |
| No/unknown    | Reference      | <.001| Reference      | <.001 |
| Yes           | .58 (.52–.65)  | <.001| .51 (.45–.58)  | <.001 |

**Abbreviations:** 95% CI, 95% confidence intervals; HR, hazard ratio.

*Figure 3.* Kaplan–Meier curves of overall survival (OS) and cancer-specific survival (CSS) in AEG patients according to marital status after matching. (A) OS curves between married and unmarried patients. (B) CSS curves between married and unmarried patients. (C) OS curves among married, single, widowed and divorced/separated patients. (D) CSS curves among married, single, widowed and divorced/separated patients.
compliance and outcome. Therefore, it is of great significance to fully understand the relationship between psychosocial factors and prognosis of tumor patients. Therefore, it is necessary to monitor the psychological changes of tumor patients and to provide more psychological care and social support for unmarried patients.

Our present findings must be interpreted in view of several limitations. First, some information related to both marital status and prognosis of AEG patients was unavailable in the SEER database, such as socioeconomic status, quality of marriage, reproductive history and subsequent therapy. However, these prognostic factors could have a major impact on the survival of AEG patients. For instance, occupation and education levels are independent prognostic factors for the survival of breast cancer patients.\textsuperscript{41-43} Moreover, higher education level is associated with improved survival of patients with prostate cancer, esophageal cancer, and non-small cell lung cancer.\textsuperscript{44-46} Despite the inaccessible information on AEG patients in the SEER database, we could rationally assume that these socioeconomic factors could influence the survival of AEG patients. Second, we only analyzed marital status at diagnosis. Marital status is not followed up after diagnosis in the SEER database, which may change after diagnosis and during anti-cancer treatment.

Conclusion

In summary, we found that married AEG patients had higher 5-year OS and CSS rates than those of unmarried ones. Widowed patients were at the highest risk of cancer-specific mortality. In addition, our study sheds light on the mechanisms of how marital status affects both OS and CSS in AEG patients with data from the large population-based SEER database. Interestingly, our results indicate that undertreatment might be one of the causes for the prognostic significance of marriage on patients, since unmarried patients were less likely to undergo surgery or chemotherapy. The underlying mechanism of the relationship between marital status and prognosis of AEG patients might be much more complicated and comprehensive. Further studies should be carried out to clarify the specific mechanisms. Finally, according to our research, greater social and psychological support should be provided to unmarried patients.

Acknowledgments

The authors are grateful for the efforts of the SEER program in creating the SEER database.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethical Statement

Since SEER database is publicly available and re-identified, approval was waived by the local ethics committee (the Second Affiliated Hospital, Zhejiang University School of Medicine) in this retrospective study. Written informed consent is not required in this retrospective analysis.

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Supplemental Material

Supplemental material for this article is available online.

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**Abbreviations**

AEG adenocarcinoma of esophagogastric junction

AJCC American Joint Committee on Cancer; CIcon confidence interval

CSS cancer-specific survival

EGJ esophagogastric junction

ESD endoscopic submucosal dissection

HPA hypothalamic–pituitary–adrenal

HR hazard ratio

IQR interquartile range

OS overall survival

PS propensity score

PSM propensity score matching

SMD standardized mean difference

SEER Surveillance, Epidemiology, and End Results