Sex Is Related to Overall Survival in Patients with Esophageal Squamous Cell Carcinoma: A Population-Based Study

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Abstract: Esophageal cancer is one of the cancers that seriously threaten the lives and health of patients around the world. Squamous cell carcinoma accounts for a higher proportion of esophageal cancer cases. At the same time, the number of esophageal squamous cell carcinoma (ESCC) patients also has an increasing trend year by year. Therefore, it is important to identify the prognostic factors of ESCC to improve the survival and prognosis of patients. As an important sociodemographic factor, gender has an important influence on the occurrence, development and prognosis of certain diseases. However, it has not been clear from existing studies whether gender affects the prognosis of ESCC patients. The aim of this study was to determine the effect of sex on overall survival (OS) in patients with ESCC. Methods: This study analyzed 6890 patients with ESCC diagnosed from 2007 to 2015 who were identified in the SEER (Surveillance, Epidemiology, and End Results) database. Kaplan-Meier method and Cox Proportional Hazards model were used to conduct survival analysis and regression analysis to evaluate the association between gender and OS. Results: We found that the OS differed with sex in patients with ESCC, with the 5-year OS rate being higher in females (19.2%) than in males (12.9%). A Cox multivariate analysis showed that sex was an independent prognostic factor for ESCC, with the OS being significantly better in female patients than in male patients ($P<0.001$). Subgroup analyses showed that sex affected the survival rate of patients with American Joint Committee on Cancer tumor, node, and metastasis stages I ($P=0.013$), II ($P<0.001$), III ($P=0.014$), and IV ($P<0.001$). Conclusion: Our results suggest that the OS of patients with ESCC is significantly better in females than males. Therefore, more attention should be paid to the prognosis of male patients with ESCC, with prospective interventions and health education applied in order to improve their survival outcomes.

Keywords: Sex, Esophageal Squamous Cell Carcinoma, Survival, Prognosis, Database

1. Introduction

Esophageal cancer is the sixth most common cause of cancer-related deaths around the world [1]. It is estimated that there are 17,650 new cases of esophageal cancer in the United States annually, with 16,080 patients with esophageal cancer dying each year [2]. Squamous cell carcinoma and adenocarcinoma are the two most common types of esophageal cancer [3]. The epidemiology of esophageal cancer in developed countries has changed recently, with adenocarcinoma surpassing squamous cell carcinoma to become the dominant type of esophageal cancer [4, 5].

However, squamous cell carcinoma still accounts for nearly 30% of cases of esophageal cancer [6]. Although the prognosis of patients with esophageal squamous cell carcinoma (ESCC) has improved due to advances in radiotherapy, chemotherapy and surgical techniques [7-9], the overall 5-year survival rate is still less than 20% [10, 11]. It is [11] therefore particularly important to identify the prognostic factors for ESCC in order to improve the survival rate of patients and the accuracy of prognoses.

As an important sociodemographics factor, sex exerts independent effects on the occurrence and development of diseases [12, 13]. Some diseases are similar between the sexes, whereas others have large sex-related differences [14, 15]. Understanding the characteristics and effects of sex in disease development is helpful for improving prevention strategies, treatments, and prognoses [12-15]. Therefore, the potential importance of sex as a demographic factor should not be neglected in patients with ESCC, especially as previous studies have shown that being female is associated with better survival outcomes in liver cancer, bladder cancer, renal pelvis cancer, and ureteral cancer [16, 17]. In addition, previous studies have shown that surgery, tumor staging, race, and other factors affect the overall survival (OS) of patients with ESCC [18]. However, the effect of sex on the prognosis of ESCC patients remains unclear.

The purpose of this research was to illustrate the effects of sex on the prognosis of ESCC patients. The research examined the impact of sex on overall survival by analyzing demographic data obtained from the Surveillance, Epidemiology, and End Results (SEER) database.

2. Material and Methods

2.1. Patient Population and Study Design

The data analyzed in this population-based survey came from the SEER program of the National Cancer Institute of the United States. The SEER database is based on data from local registries in 19 regions of the country, covering about 28% of the population of the United States, and contains information on all event cases such as general demographic information as well as information on tumor characteristics, treatment, and survival [19, 20]. The population covered by the SEER database is highly representative of the total population of the United States [21].

We identified 6890 patients with ESCC in the SEER database who had been diagnosed between 2007 and 2015. The following SEER variables were used to identify patients: "Site Recode ICD-O-3/WHO 2008 classification" (esophagus) and "Histology recode-broad groupings" (histology codes: 8050–8089). The study only included patients with well-documented follow-up data; those with imperfect data registration or a first primary cancer that was not ESCC were excluded.

This study included insurance status as a variable, but since insurance status was first reported by the SEER program in 2007, we included only patients who were first diagnosed between 2007 and 2015 and for whom there were complete insurance records in the database. Based on the information in the SEER database, we classified the insurance status into insured, Medicaid, and uninsured. The marital status is divided into married (common-law marriage) and unmarried (including widowed, divorced, separated, unmarried, and single patients, and those with a domestic partner who they were not married to).

2.2. Study Variables

We retrieved the following data from the SEER: sex (female or male), age [three groups based on the following optimal cutoff values identified according to the X-tile program (Yale University version 3.6.1): ≤71, 72–79, or ≥80 years], race (white, black, or other), year of diagnosis (2007–2009, 2010–2012, or 2013–2015), tumor grade (I, well differentiated; II, moderately differentiated; III, poorly differentiated; or IV, undifferentiated), sixth edition of the American Joint Committee on Cancer tumor, node, and metastasis (AJCC TNM) staging system (stage I, II, III, or IV), surgery (yes or no), tumor size (<2, 2–4, or >4 cm, or unknown), marital status (married or unmarried), and insurance status (insured, Medicaid, or uninsured). Data on follow-up time and life status were also included. The above variables were analyzed statistically, and variables for which $P<0.1$ in the univariate analyses were included in a Cox multivariate analysis.

2.3. Statistical Analyses

To facilitate comparisons of the characteristics of patients, mean±standard deviation values were used to represent continuous variables. Continuous variables that conformed to a nonnormal distribution were compared using Student's *t* test, while Pearson's χ^2 test was used to compare classified variables. OS was the primary end point, and was defined as the time from the diagnosis of ESCC to death. OS was calculated using the Kaplan-Meier graphic method, and the differences between groups in these diagrams were compared using logarithmic rank test. Cox regression models were used to determine which of the following variables were related to OS: sex, race, age, year of diagnosis, tumor grade, AJCC TNM stage, surgery status, tumor size, insurance status, and marital status. The optimal cutoff points for age were determined using minimum probability value from log-rank χ^2 statistics with the aid of the X-tile program, which resulted in age groups of ≤71, 72–79, and ≥80 years being included in the Cox multivariate analysis.

All of the statistical tests were bilateral, and differences were considered to be statistically significant when $P<0.05$. SPSS (version 20.0, SPSS, Chicago, Illinois, USA) was used for all of the statistical analyses.

3. Results

3.1. Baseline Characteristics

Table 1 lists the baseline characteristics of the 6890 analyzed patients stratified by sex: the 2417 (35.08%) females

and 4473 (64.92%) males had median ages of 69 and 66 years, respectively. Compared to the females, more of the males were married (52.60% vs. 39.70%) and white (70.70% vs. 62.00%), whereas more of the female patients had received surgery (20.60% vs. 17.00%). There were significant sex-related differences in age ($P<0.001$), race ($P<0.001$), tumor grade ($P<0.01$), AJCC TNM stage ($P<0.001$), surgery status ($P<0.001$), insurance status ($P<0.001$), and marital status ($P<0.001$).

***Table 1.** Patient and tumor characteristics of patients with Esophageal squamous cell carcinoma, SEER 2007-2015.*

Characteristic	Total	Female	Male	P-value
Patients, n (%)	6890 (100.00)	2417 (35.08)	4473 (64.92)	
Age, mean ± SD		68.75±11.58	66.44±10.78	<0.001
Race (%)				<0.001
White	4484 (65.10)	1709 (70.70)	2775 (62.00)	
Black	1722 (25.00)	528 (21.80)	1194 (26.70)	
Other	684 (9.90)	180 (7.40)	504 (11.30)	
Year (%)				0.884
2007-2009	2324 (33.70)	809 (33.50)	1515 (33.90)	
2010-2012	2314 (33.60)	809 (33.50)	1505 (33.60)	
2013-2015	2252 (32.70)	799 (33.00)	1453 (32.50)	
Grade (%)				0.001
I	409 (5.90)	145 (6.00)	264 (5.90)	
II	3399 (49.30)	1272 (52.60)	2127 (47.60)	
III	3020 (43.80)	979 (40.50)	2041 (45.60)	
IV	62 (0.90)	21 (0.90)	41 (0.90)	
AJCC TNM stage (%)				<0.001
I	1166 (16.90)	474 (19.60)	692 (15.50)	
II	1720 (25.00)	678 (28.10)	1042 (23.30)	
III	1853 (26.90)	648 (26.80)	1205 (26.90)	
IV	2151 (31.20)	617 (25.50)	1534 (34.30)	
Surgery (%)				<0.001
Yes	1256 (18.20)	497 (20.60)	759 (17.00)	
No	5634 (81.80)	1920 (79.40)	3714 (83.00)	
Tumor size (%)				0.763
<2cm	4531 (65.80)	1607 (66.50)	2924 (65.40)	
2-4cm	14 (0.20)	4 (0.20)	10 (0.20)	
>4cm	161 (2.30)	57 (2.40)	104 (2.30)	
Unknown	2184 (31.70)	749 (31.00)	1435 (32.10)	
Insurance status (%)				<0.001
Insured	5268 (76.50)	1921 (79.50)	3347 (74.80)	
Medicaid	1322 (19.20)	415 (17.20)	907 (20.30)	
Uninsured	300 (4.40)	81 (3.40)	219 (4.90)	
Marital status (%)				<0.001
Married	3311 (48.10)	959 (39.70)	2352 (52.60)	
Unmarried	3579 (51.90)	1458 (60.30)	2121 (47.40)	

AJCC, American Joint Committee on Cancer; SD, standard deviation; TNM, tumor, node, and metastasis.

3.2. Survival Analysis

3.2.1. Sex and OS

The Kaplan-Meier curves for the OS in Figure 1 shows that the survival rate varied with sex ($P<0.001$). The median survival time was longer for female patients (12 months) than for male patients (9 months). Similarly, females have a higher 5-year OS ratio than males (19.2% vs. 12.9%). In the univariate analyses, all variables were found to be significant predictors of OS. After adjustment in the multivariate analysis, the variables remained independent and significant except for race (other, $P=0.417$), tumor grade (IV, $P=0.671$), and tumor size (2–4 cm, $P=0.551$). Being male had a significant negative effect on the survival outcome (hazard ratio [HR]=1.237, 95% confidence interval [CI]=1.166–1.313, $P<0.001$) (Detailed see Table 2).

Table 2. *Cox Univariate and multivariate survival analysis of OS in patients with Esophageal squamous cell carcinoma (ESCC).*

Characteristic	Univariate analysis			Multivariate analysis		
	HR	95% CI	P-value	HR	95% CI	P-value
Age, years						
≤71	Reference			Reference		
72-79	1.105	1.032-1.183	0.004	1.191	1.111-1.278	<0.001
≥80	1.472	1.366-1.587	<0.001	1.574	1.454-1.704	<0.001
Race						
White	Reference			Reference		
Black	1.301	1.222-1.384	<0.001	1.140	1.066-1.220	<0.001
Other	1.014	0.923-1.114	0.774	1.040	0.946-1.145	0.417
Gender						
Female	Reference			Reference		
Male	1.248	1.178-1.322	<0.001	1.237	1.166-1.313	<0.001
Year of diagnosis						
2007-2009	Reference			Reference		
2010-2012	0.916	0.860-0.975	0.006	0.931	0.874-0.992	0.026
2013-2015	0.882	0.822-0.948	0.001	0.906	0.843-0.973	0.007
Grade						
I	Reference			Reference		
II	1.444	1.269-1.644	<0.001	1.278	1.122-1.456	<0.001
III	1.686	1.481-1.920	<0.001	1.347	1.182-1.536	<0.001
IV	1.366	1.003-1.860	0.048	1.069	0.784-1.458	0.671
AJCC TNM stage						
I	Reference			Reference		
II	0.830	0.759-0.908	<0.001	0.864	0.790-0.946	0.002
III	1.138	1.044-1.240	0.003	1.187	1.087-1.296	<0.001
IV	2.198	2.024-2.386	<0.001	1.936	1.778-2.107	<0.001
Surgery						
Yes	Reference			Reference		
No	2.616	2.412-2.838	<0.001	1.988	1.827-2.164	<0.001
Tumor size						
<2cm	Reference			Reference		
2-4cm	1.099	0.608-1.986	0.755	1.198	0.661-2.169	0.551
>4cm	1.435	1.205-1.709	<0.001	1.242	1.042-1.479	0.016
Unknown	1.269	1.198-1.345	<0.001	1.121	1.057-1.189	<0.001
Insurance status						
Insured	Reference			Reference		
Medicaid	1.220	1.139-1.306	<0.001	1.106	1.028-1.190	0.007
Uninsured	1.476	1.299-1.679	<0.001	1.348	1.181-1.539	<0.001
Marital status						
Married	Reference			Reference		
Unmarried	1.294	1.225-1.366	<0.001	1.206	1.138-1.279	<0.001

HR, hazard ratio; CI, confidence interval; AJCC, American Joint Committee on cancer; TNM, tumor, node, and metastasis.

Table 3. *Cox Univariate and multivariate survival analysis of patients with esophageal squamous cell carcinoma (ESCC) based on age.*

Characteristic	5-year survival, %	Median survival time, months	Univariate analysis		Multivariate analysis		
			Log rank χ2	P-value	HR	95% CI	P-value
≤71 years			75.960	<0.001			
Female	23.3	15			Reference		
Male	14.4	9			1.330	1.231-1.437	<0.001
72-79 years			8.193	0.004			
Female	16.1	11			Reference		
Male	10.7	9			1.158	1.021-1.314	0.022
≥80 years			1.560	0.212			
Female	10.9	6			Reference		
Male	7.9	6			1.076	0.931-1.243	0.322

HR, Full name is hazard ratio; CI, Full name is confidence interval.
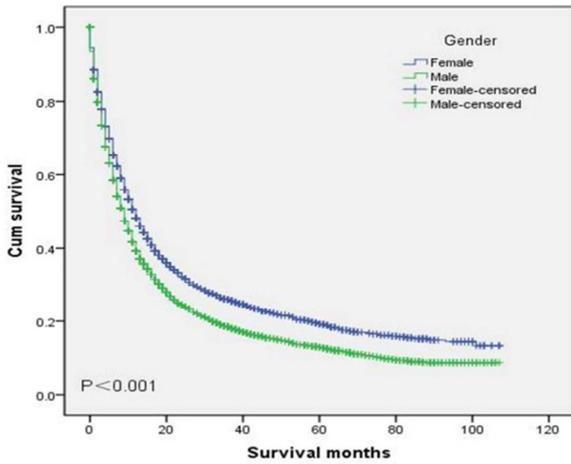
Figure 1. *Kaplan-Meier (KM) survival curves of patients with esophageal squamous cell carcinoma (ESCC), SEER 2007-2015 by gender status. Cum, cumulative.*
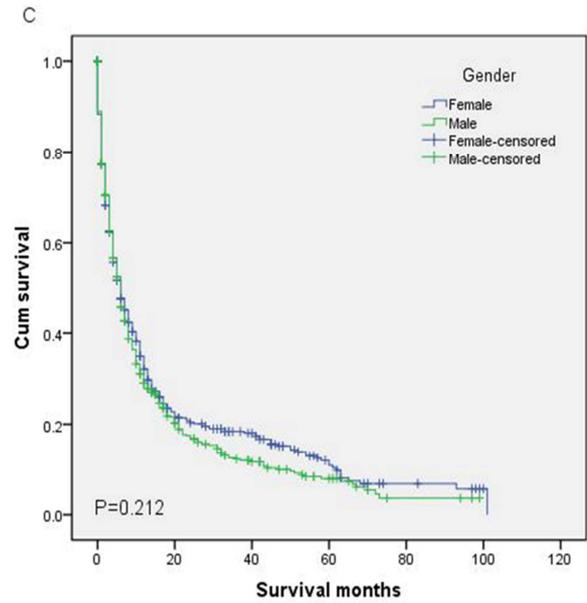

Figure 2. *Kaplan-Meier (KM) Survival curves in different age subgroups of patients with esophageal squamous cell carcinoma (ESCC) according to gender status. (A) ≤71 years OS. (B) 72-79 years OS. (C) ≥80 years OS. OS, overall survival; Cum, cumulative.*
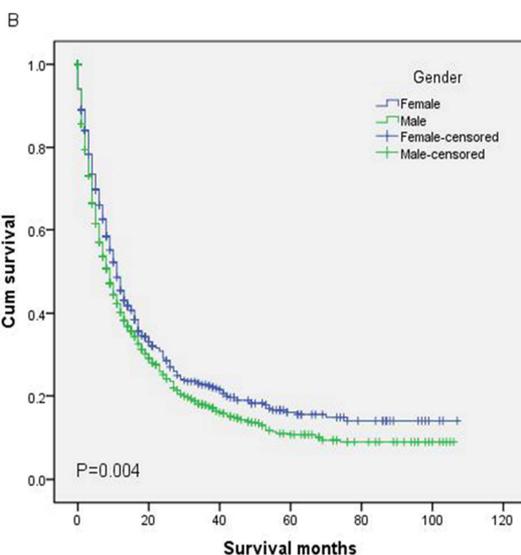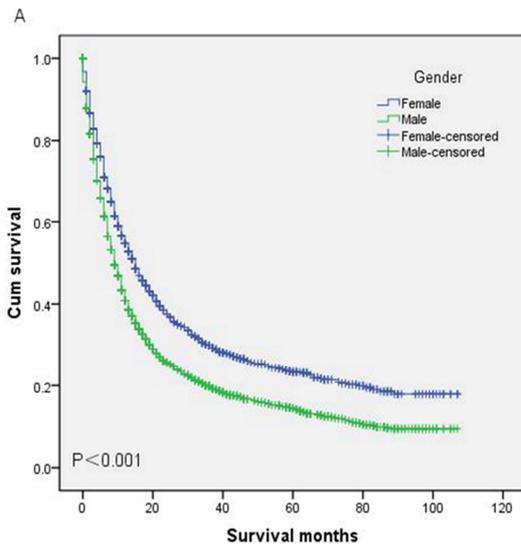
3.2.2. Subgroup Analyses of the Effect of Sex According to Age

Figure 2 illustrates the Kaplan-Meier (KM) survival curves for sex and age. The 5-year OS rate was higher in females than in males for patients aged ≤71 years (23.3% vs. 14.4%, $P<0.001$) and 72–79 years (16.1% vs. 10.7%, $P=0.004$), whereas it did not differ with sex in those aged ≥80 years ($P=0.212$). Cox Multivariate analysis showed that sex affected the OS in those patients aged ≤71 years (HR=1.330, 95% CI=1.231–1.437, $P<0.001$) and 72–79 years (HR=1.158, 95% CI=1.021–1.314, $P=0.022$) (Detailed see Table 3).

3.2.3. Subgroup Analyses of the Effects of Sex According to Surgery Status

Figure 3 shows the Kaplan-Meier survival curves for sex and surgery. The 5-year OS rate was higher in female than male patients both in those who received surgery (43.1% vs. 33.7%, $P=0.001$) and who did not receive surgery (13.1% vs. 8.4%, $P<0.001$). Multivariate analysis showed that sex affected OS in both surgical recipients (HR=1.274, 95% CI=1.038–1.499, $P=0.003$) and non-recipient patients (HR=1.221, 95% CI=1.146–1.302, $P<0.001$) (Detailed see Table 4).

3.2.4. Subgroup Analyses of the Effect of Sex According to AJCC TNM Stage

Figure 4 clearly shows Kaplan-Meier (KM) survival curves for male and female ESCC patients in AJCC TNM stage I (n=1166), stage II (n=1720), stage III (n=1853), and stage IV (n=2151). The 5-year OS rate was higher in females than in males for patients at AJCC TNM stage II (29.2% vs. 20.2%, $P<0.001$), stage III (18.9% vs. 14.0%, $P=0.016$), and stage IV (5.2% vs. 3.0%, $P<0.001$), while there was no sex-related

difference for stage I. Cox multivariate analysis indicated that sex was a significant independent prognostic factor for OS in ESCC patients with different AJCC TNM stages, not only at stage I (HR=1.202, 95% CI=1.040–1.388, *P*=0.013), stage II

(HR=1.337, 95% CI=1.179–1.516, *P*<0.001), but also at stage III (HR=1.156, 95% CI=1.030–1.298, *P*=0.014), and stage IV (HR=1.268, 95% CI=1.145–1.404, *P*<0.001) (Detailed see Table 5).
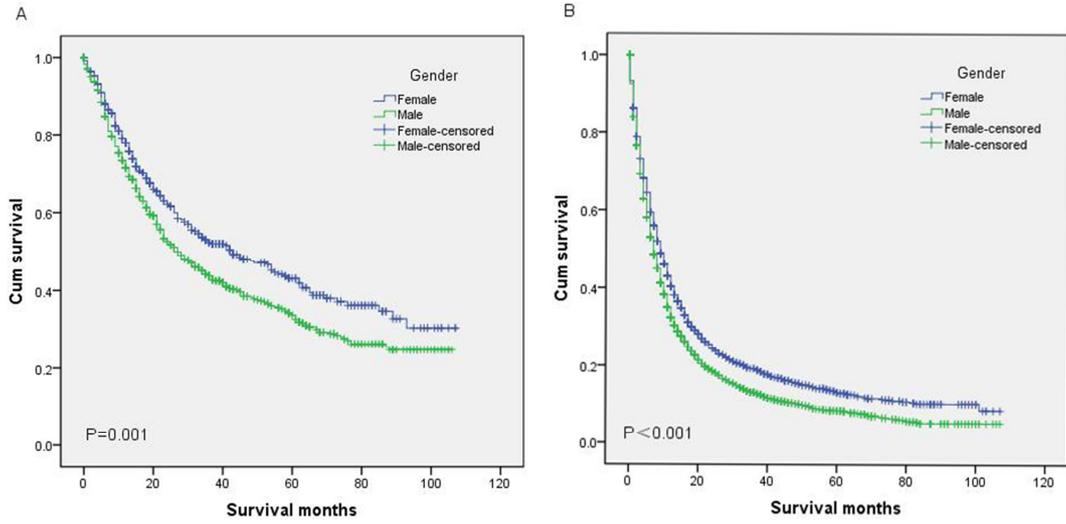

Figure 3. *Survival curves in different surgery subgroups of patients with esophageal squamous cell carcinoma according to gender status. (A) Surgery OS. (B) No surgery OS. OS, overall survival; Cum, cumulative.*
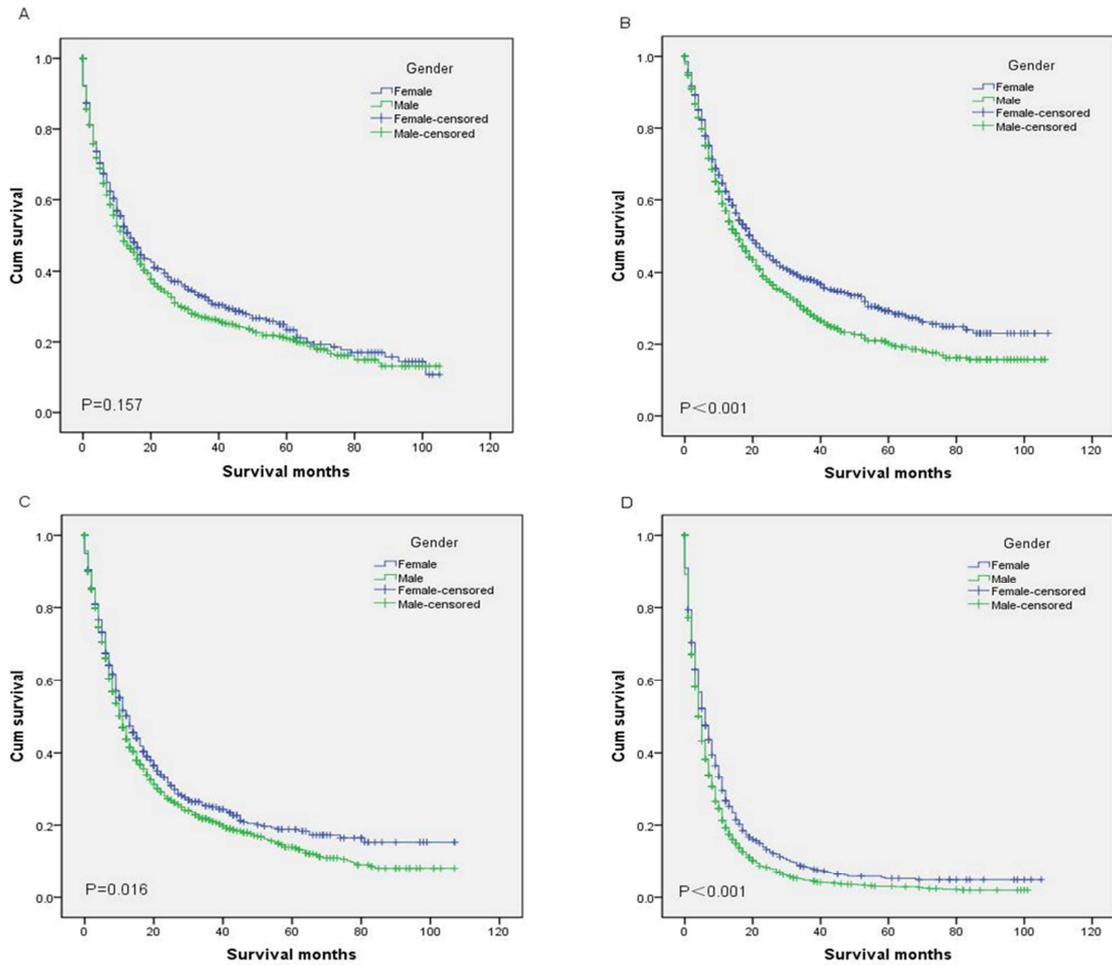

Figure 4. *According to different gender status, survival curves of ESCC patients with different tumor Tumor-Node-Metastasis stage subgroups were obtained by survival analysis. (A) Stage I OS. (B) Stage II OS. (C) Stage III OS. (D) Stage IV OS. OS, overall survival; Cum, cumulative.*

Table 4. *Univariate and multivariate survival analysis of patients with esophageal squamous cell carcinoma (ESCC) according to surgery details.*

Characteristic	5-year survival, %	Median survival time, months	Univariate analysis		Multivariate analysis		
			Log rank χ2	P-value	HR	95%CI	P-value
Surgery			10.127	0.001			
Female	43,1	43			Reference		
Male	33.7	27			1.274	1.038-1.499	0.003
No surgery			40.176	<0.001			
Female	13.1	9			Reference		
Male	8.4	7			1.221	1.146-1.302	<0.001

HR, Full name is hazard ratio; CI, Full name is confidence interval.

Table 5. *Cox regression univariate and multivariate survival analyses of patients with esophageal squamous cell carcinoma (ESCC) according to the Cancer Tumor- Node-Metastasis stage of American Joint Committee.*

Characteristic	5-year survival, %	Median survival time, months	Univariate analysis		Multivariate analysis		
			Log rank χ2	P-value	HR	95% CI	P-value
			2.005	0.157			
Female	23.4	14			Reference		
Male	21.0	12			1.202	1.040-1.388	0.013
II			12.175	<0.001			
Female	29.2	20			Reference		
Male	20.2	16			1.337	1.179-1.516	<0.001
III			5.825	0.016			
Female	N/A	13			Reference		
Male	14.0	11			1.156	1.030-1.298	0.014
IV			17.844	<0.001			
Female	5.2	6			Reference		
Male	3.0	5			1.268	1.145-1.404	<0.001

HR, Full name is hazard ratio; CI, Full name is confidence interval.

4. Discussion

This study investigated the relationship between sex and OS in patients with ESCC in the United States. Univariate and multivariate analyses revealed that the incidence of OS was higher in female patients than in male patients, suggesting that sex is an important independent prognostic factor for the survival of patients with ESCC. The results of our research are similar to those of previous studies that analyzed data in the SEER database to explore the relationship between sex and survival in patients with liver cancer [16]. Westwick et al. found that the mortality rate of patients with spinal meningioma was higher in males than in females, which also supports the results of the present study [22]. The sex-related difference in survival rate might be related to differences in hormone levels, since estrogen and progesterone in females can reportedly reduce their risk of developing ESCC [23], and overexpression of the androgen receptor is related to the occurrence of ESCC and adenocarcinoma [24].

The prognosis of cancer patients differs significantly with age [25, 26], and so we performed subgroup analyses of the effects of sex on patients with ESCC at different ages. The results showed that among patients with ESCC aged ≤71 and 72–79 years, females had a significant survival advantage over males, whereas the OS did not differ between male and female patients aged ≥80 years. The sex-related difference in survival rate among patients aged ≤79 years may be due to better compliance behaviors of females compared with males [27], while patients aged 70–80 years have lower tumor invasiveness, resulting in prognoses that are more similar to

those of young people [28]. However, both female and male patients aged ≥80 years were found to have significantly increased mortality due to their poor functional status [29], which could explain the absence of a difference in OS between males and females in that age group.

Some previous studies have shown that surgical resection is associated with better survival in patients with ESCC [7], whereas Chang et al. reported that treatments such as surgery do not affect the OS of these patients [30]. These two contrasting findings explain why we conducted subgroup analyses of the effects of surgery on sex. Our results show that sex is not only an independent prognostic factor for patients who receive surgery with OS, but also an independent prognostic factor for those who do not receive surgery. Therefore, sex is a protective factor for both ESCC patients who have received surgery and those who have not, which should be paid attention to.

Zhong et al. found that AJCC TNM stages II and III were related to the survival of ESCC patients, which may be closely related to lymph node dissection [31]. However, the subgroup analyses of AJCC TNM staging performed in the present study showed that sex is an independent prognostic factor for OS in patients at all four stages (I, II, III, and IV). Therefore, sex is a protective factor not only for patients with mid-term ESCC, but also for those with early and late ESCC, and its influence can therefore not be ignored.

Despite insurance status being closely related to the prognosis of patients [32], most previous studies have not included insurance status when investigating the factors that affect the prognosis of ESCC [33]. Therefore, the present

study included insurance status in order to more-comprehensively analyze the important factors that affect the prognosis of ESCC patients. This study found that insurance status is a meaningful independent prognostic factor for the survival of patients with ESCC. Compared with insured patients, the risk of death is higher for Medicaid patients (HR=1.106, 95% CI=1.028–1.190, P=0.007) and uninsured patients (HR=1.348, 95% CI=1.181–1.539, P<0.001). These findings might be due to the socioeconomic status being better for patients who purchase insurance than for uninsured patients, and they are consistent with the findings of Wang et al. [19] and Perry et al. [32].

To the best of our knowledge, the present research is the first population-based research to explore the association between sex and OS in patients with ESCC. Afshar et al. found that female patients have a higher risk of death and a lower survival rate than male patients with bladder cancer, renal pelvis cancer, and ureteral cancer; however, that study did not include patients with ESCC [17]. Our results showed that in a cohort of patients with ESCC, the survival time was significantly longer and the OS rate was significantly higher in females than in males.

There are multiple possible factors underlying why female ESCC patients show better survival. A much lower proportion of female patients than male patients drink alcohol and smoke [34, 35], and both drinking and smoking increase the risk of ESCC [36]. Smoking can cause oxidative stress and DNA damage in the body, and cigarettes release carcinogens such as nitrosamines and damaging aromatic hydrocarbons during combustion, which increase the risk of esophageal cancer [37, 38]. Drinking alcohol can inhibit the activity of natural killer cells and promote tumor metastasis [39]. In addition, tobacco and alcohol can produce focal disturbances in the expression of 27-kDa heat shock protein in the esophagus, which can promote the occurrence of ESCC [40]. Male patients, with their higher rates of smoking and drinking alcohol [41], will potentially be more affected by lasting damage to the esophagus, which will affect the effectiveness of treatment and prognosis to varying degrees. These reasons can explain why the OS rate of male patients with ESCC is lower than that of female patients with ESCC.

We also found that the proportion of patients receiving surgery was higher among females than males. The surgery status is an important factor for improving the survival time of patients with ESCC [3, 7], since surgery can involve removing tumors from primary or distant metastatic sites, and performing lymph node dissection. Haisley et al. found that each 1-cm increase in tumor length decreasing OS (HR=1.18, 95% CI=1.06–1.32, P =0.003) [42]. Surgical resection can also inhibit tumor progression [3, 7]. In addition, studies have shown that the survival advantage of female cancer patients over male cancer patients is closely related to their higher treatment compliance and better health behaviors [27], while a lower acceptance rate of surgery, treatment compliance, and healthy behaviors reduce the survival potential of male patients [3, 7, 27]. Our results suggest that it is not enough to focus on differences in cancer survival at the levels of age, surgery, radiotherapy, and chemotherapy; instead, there is an urgent need to also pay attention to sex differences in survival among patients with ESCC. Early screening, guidance, and assistance are needed

for improving the OS of high-risk male patients with ESCC.

Some limitations of the current research should be considered. First, the SEER data registry has limitations in providing information about patients and does not report any comorbidities or complications [43]. Second, the SEER database temporarily not provided specific information about radiotherapy, chemotherapy, or drug use [18], and these variables will certainly affect the prognosis of patients with ESCC. Future studies should attempt to adjust for these covariates in order to obtain more-comprehensive results. Third, the income and education levels of individual patents are not available in the SEER database, and both of these factors may affect treatment choices [19]. Fourth, the SEER database does not record poor habits in the daily lives of patients, such as drinking alcohol and smoking. These two factors are closely related to the prognosis of patients with ESCC [44], but we could not include them in this study. Finally, our study had a short follow-up, which was due to data on the insurance status only being added to the SEER database in 2007, and the data only being available up to 2015. Longer follow-up periods are needed in future studies to verify whether the present results also apply over longer time periods.

Notwithstanding the aforementioned potential limitations, the present findings suggest that being female is associated with better survival in patients with ESCC, independent of the other analyzed variables. Our results clearly indicate that particular focus needs to be placed on male patients diagnosed with ESCC, and prospective prognostic interventions and health education should be applied to improve their survival. In addition, early and active screening is recommended for males with other risk factors for ESCC.

5. Conclusion

Female ESCC patients have significantly better OS than men. Sex is an independent prognostic factor for ESCC.

Currently, it is generally accepted that female patients with ESCC have a better survival rate than male patients because the proportion of drinking and smoking among female patients is much lower than that of male patients, which reduces the risk of female patients with ESCC to some extent and is more conducive to their recovery after the disease.

Women's better treatment compliance and health behaviors, as well as their higher surgical acceptance rate, are important reasons for the higher survival rate of women with ESCC than men.

Prospective intervention measures and health education for male ESCC patients are particularly important to reduce their mortality and improve their prognosis.

Current Research Questions

What are the barriers to early screening and intervention for male ESCC patients?

How to implement early intervention to reduce the mortality rate of male ESCC patients?

Can early comprehensive intervention effectively improve the prognosis of patients with advanced ESCC?

Contributorship Statement

Qiao-hong Yang: Conceptualization, Methodology, Project administration. Yao-xia Li and Na Wang: Software, Data curation, Writing-Original draft preparation. Jia-le Wang and Jun Lyu: Visualization, Supervision, Investigation. Zhuo-rui Zhao, Qin-yang Wu and Qi-qi Ke: Supervision, Writing-Reviewing and Editing.

Competing Interests

All the authors do not have any possible conflicts of interest.

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