European Journal of Surgical Oncology 45 (2019) 1969–1976

Contents lists available at ScienceDirect

European Journal of Surgical Oncology

journal homepage: www.ejso.com

Incidence and risk factors for suicide death in male patients with genital-system cancer in the United States

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ARTICLE INFO

Article history:
Accepted 14 March 2019
Available online 19 March 2019

Keywords:
Genital-system cancer
Suicide
Incidence
Risk factors
SEER

ABSTRACT

Background: A diagnosis of cancer is associated with increased risks of suicidal ideation and suicide attempts. Genital-system cancer comprises nearly a third of all cancers in males. We used the SEER database to identify the incidence of and risk factors for suicide death in male patients with genital-system cancer in the United States.

Method: Patients were selected from the SEER database, and X-tile software was used to find the best cutoffs for stratifying age. Logistic regression was used to identify independent risk factors for suicide death. Only variables that were statistically significant in the univariate logistic regression models were analyzed in multivariate logistic regression models.

Result: This study found that age (18–66 vs ≥ 76 years: OR = 3.300, $P < 0.001$; 67–75 vs ≥ 76 years: OR = 1.832, $P < 0.001$), being unmarried (OR = 1.332, $P = 0.010$), being divorced, separated, or widowed (OR = 1.338, $P = 0.002$), caucasian (OR = 2.074, $P = 0.003$) and not receiving surgery or having an unknown surgery status (OR = 1.405, $P < 0.001$) significantly increased the risk of suicide death. A particularly important finding was that a time of <1 year after the diagnosis was related to an increased risk of suicide death (<1 vs ≥ 10 years: OR = 1.761, $P = 0.008$).

Conclusion: We found that a number of factors significantly increased the risk of suicide. Importantly, a time of <1 year after the diagnosis was related to an increased risk of suicide death, which indicates the importance of identifying and treating people at risk of suicide as early as possible. These can help clinicians to understand suicidal patients and provide them with appropriate support.

Introduction

Suicide is one of the leading causes of death and disability worldwide and is the tenth most common cause of death in the United States [1–4]. Cancer is a major disease that seriously threatens human life both physically and mentally [5,6], and a diagnosis of cancer is associated with increased risks of suicidal ideation and suicide attempts [7–9]. Previous studies have shown that the suicide rate among cancer patients is almost double that in the general population [10–12], which is mainly due to anxiety, comorbidities, psychosocial conditions, and the decline in quality of life caused by adverse drug reactions [13–16].

Male genital-system cancer (MGSC) comprises nearly a third of all cancers in males [17]. Prostate cancer is the most commonly diagnosed MGSC and the second leading cause of all cancer-related deaths, testicular cancer is the most common solid tumor among

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https://doi.org/10.1016/j.ejso.2019.03.022

Table 1
Characteristics of patients.

Variables	Suicide [n (%)]	No suicide [n (%)]
Age at diagnosis	67 ± 0.37	72 ± 0.03
Marital status		
Married	444 (62.8)	61461 (68.1)
Unmarried	103 (14.6)	10483 (11.6)
DSW	160 (22.6)	18260 (20.2)
Race		
Caucasian	650 (91.9)	71591 (79.4)
Black	40 (5.7)	14479 (16.1)
Other	17 (2.4)	4134 (4.6)
Primary site		
prostate	706 (99.9)	90108 (99.9)
testis	1 (0.1)	96 (0.1)
AJCC stage		
I	3 (0.4)	303 (0.3)
II	604 (85.4)	69513 (77.1)
III	41 (5.8)	4916 (5.4)
IV	59 (8.3)	15472 (17.2)
Surgery		
Yes	292 (41.3)	26233 (29.1)
NO/Unknown	415 (58.7)	63971 (70.9)
Radiation		
Yes	234 (33.1)	34313 (38.0)
NO/Unknown	473 (66.9)	55891 (62.0)
Insurance status		
Insured	157 (94.0)	15610 (88.3)
Uninsured	1 (0.6)	399 (2.3)
Any medicaid	9 (5.4)	1664 (9.4)
Survival months	47 ± 1.29	51 ± 0.11

Abbreviations: DSW, divorced & separated &widowed. AJCC stage, American Joint Committee on Cancer (AJCC) staging.

males aged 15–34 years, while penile and other MGSCs are uncommon [17]. Although there have been reports that prostate and penile cancers are related to suicide death [18,19]. There has been no report on the relationship between cancer and suicide death from the perspective of the male genital system as a whole.

The purpose of this study was to use the SEER database to identify the incidence of and risk factors for suicide death in MGSC patients in the United States. The SEER database may be a useful resource for identifying more suicide cases since it includes 18 registries that cover 30% of the United States population and collects demographic, clinical, and outcome information on all cancers diagnosed in representative geographic regions and subpopulations of the United States [20,21].

Methods

Patients

We searched the SEER database for records from 2004 to 2015 using the following ICD-O-3 primary-site codes: C60.0-C60.2, C60.8, C60.9, C61.9, C62.0, C62.1, C62.9, C63.0–C63.2, and C63.7–C63.9. All of the included patients were older than 18 years. People who died of any cause were included, and those within this population who had suicided were identified. Cases without a diagnosis, or microscopic confirmation, only with autopsy findings, or incomplete variables were excluded. The following information was collected for each patient: age at diagnosis, marital status, race, primary site, American Joint Committee on Cancer (AJCC) staging, surgery status, radiation status, insurance status, survival period, and cause of death. The application of our selection criteria identified 90911 eligible patients, of whom 707 had suicided.

Statistical analysis

Patients were divided into the following two groups: suicide and no suicide. Continuous variables that conformed to a normal distribution were expressed as mean ± standard-deviation values, while categorical variables were expressed as percentages. Logistic regression was used to identify independent risk factors for suicide death. Only variables that were statistically significant in the univariate logistic regression models were analyzed in multivariate logistic regression models.

Age was the only continuous variable. To explore the risk of suicide among patients of different ages, we used X-tile software to find the best cutoffs for stratifying age. The use of data in the SEER database does not require informed patient consent because the patients were anonymized and de-identified prior to release. The SEER database can be accessed free of charge, and this study was exempted from obtaining informed consents by the institutional research committee of the First Affiliated Hospital of Xi'an Jiaotong University.

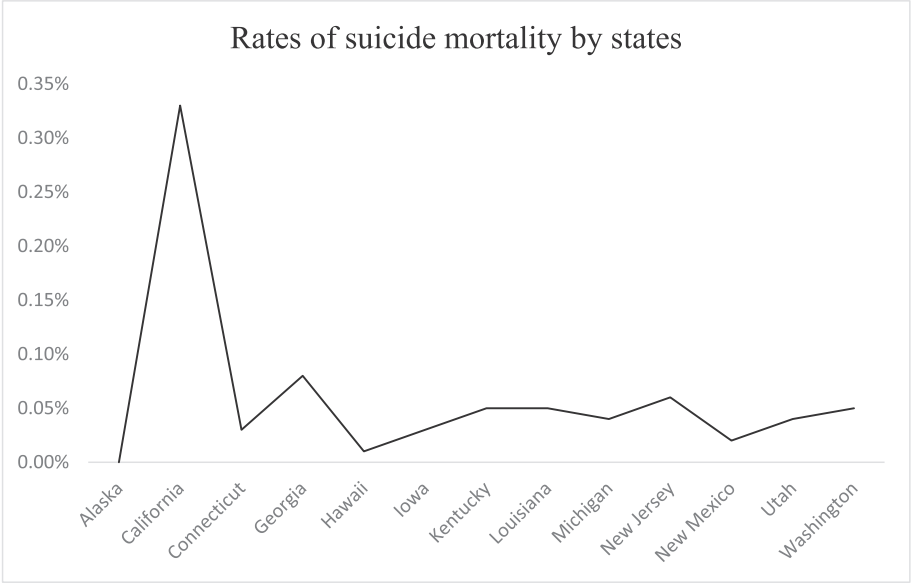

Fig. 1. Rates of suicide mortality by states.

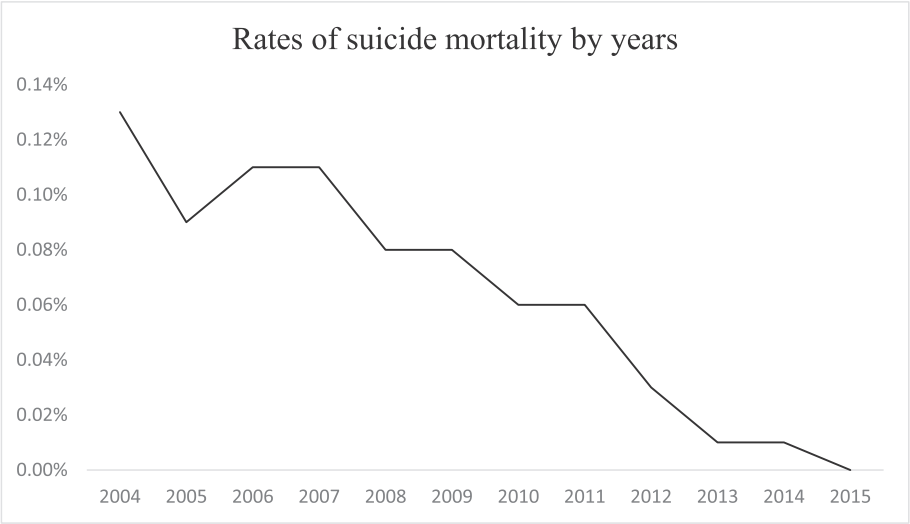

Fig. 2. Rates of suicide mortality by years.

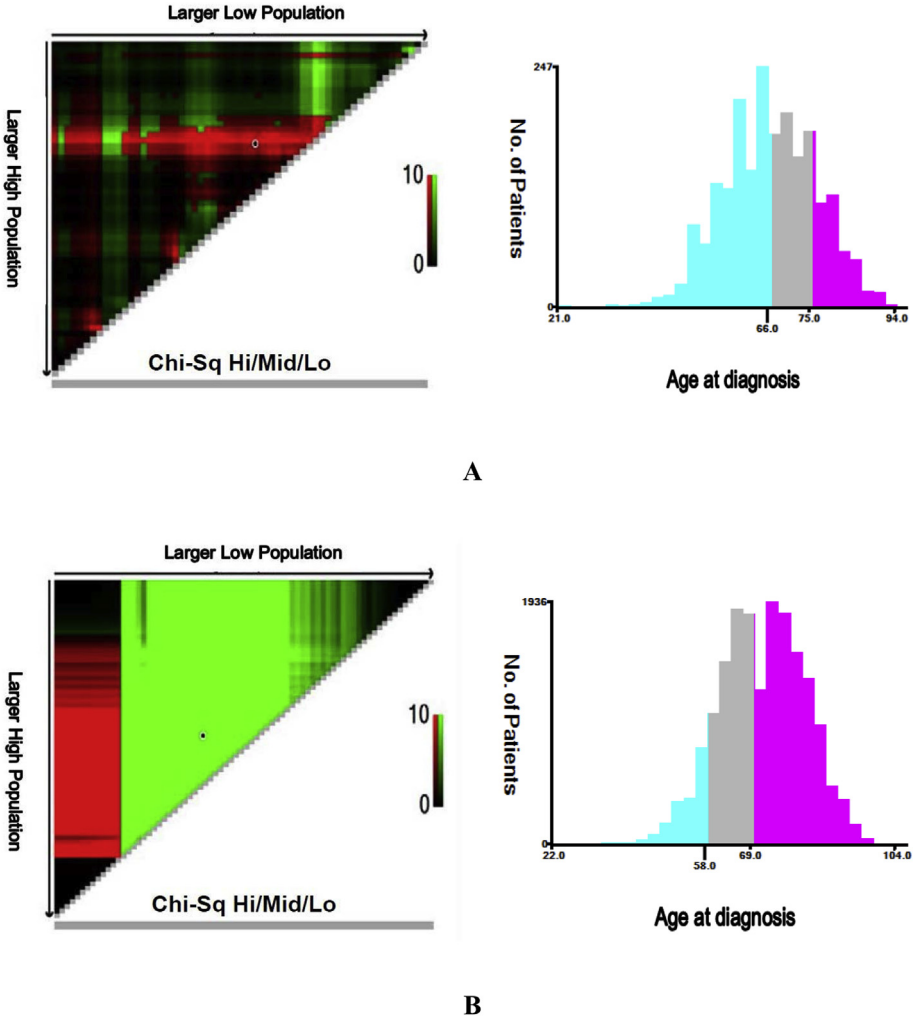

Fig. 3. Age at diagnosis stratification by X-tile software. A:2004–2015 B:2010–2015.

All statistical tests were two sided, with $P < 0.05$ considered to be indicative of statistical significance. All statistical analyses were performed using SPSS (version 24.0, SPSS, Chicago, IL, USA). The X-tile program was implemented using X-tile software (http://tissuearray.org/).

Results

Baseline patient characteristics

The baseline demographics in the two groups are presented in Table 1. Most of the patients in the present cohort were married, were caucasian, had prostate cancer, had AJCC stage II, had not received surgery or had an unknown surgery status (henceforth referred to as no/unknown surgery), had not received radiation therapy or had an unknown radiation therapy status, and were insured. The mean ages at the cancer diagnosis in the suicide and no-suicide cohorts were 67 and 72 years, respectively. Among the 707 patients who suicided, the death rate was highest in California, at 0.33%, followed by Georgia and New Jersey at 0.08% and 0.06%, respectively (Fig. 1). In terms of time, the suicide death rate was highest in 2004, at 0.13%, declining to 0.09% in 2005 and then increasing in 2006 to 0.11%, and continuing to increase into 2007. However, there was an overall declining trend in the rate of suicide death (Fig. 2).

Risk factors for suicide death during 2004–2015

We included all of the study variables in the univariate logistic regression analysis. X-tile software was used to identify the following optimal cutoffs for the age at diagnosis: 18–66, 67–75, and ≥76 years (Fig. 3A). Multivariate logistic regression was then performed that included those factors that were significant in the univariate analysis. As listed in Table 2, age (18–66 vs ≥ 76 years: odds ratio [OR] = 3.300, 95% confidence interval [CI] = 2.707–4.002, $P < 0.001$; 67–75 vs ≥ 76 years: OR = 1.832, 95% CI = 1.485–2.260, $P < 0.001$), marital status (unmarried vs married: OR = 1.332, 95% CI = 1.069–1.659, $P = 0.010$; divorced, separated, or widowed [DSW] vs married: OR = 1.338, 95% CI = 1.114–1.606, $P = 0.002$), caucasian (vs another race: OR = 2.074, 95% CI = 1.279–3.361, $P = 0.003$), and surgery (no/unknown vs yes: OR = 1.405, 95% CI = 1.187–1.664, $P < 0.001$) significantly increased the risk of suicide death. Finally, a time of <1 year after the diagnosis was also related to an increased risk of suicide death (<1 vs ≥ 10 years: OR = 1.761, 95% CI = 1.157–2.680, $P = 0.008$).

Subanalysis of patients diagnosed from 2010 to 2015

The insurance status was only recorded in the SEER database after 2007, and the 7th edition of the American Joint Committee on Cancer (AJCC) staging system was recorded in 2010. This subset of

Table 2
Univariate and multivariate logistic regression analysis from 2004 to 2015.

Variables	Univariate analysis			Multivariate analysis		
	OR	95%CI	*P*-value	OR	95%CI	*P*-value
Age at diagnosis						
18–66	3.010	2.483–3.649	<0.001	3.300	2.707–4.002	**<0.001**
67–75	1.660	1.349–2.014	<0.001	1.832	1.485–2.260	**<0.001**
≥76	Reference			Reference		
Marital status						
Married	Reference			Reference		
Unmarried	1.360	1.097–1.687	0.005	1.332	1.069–1.659	**0.010**
DSW	1.213	1.012–1.454	0.037	1.338	1.114–1.606	**0.002**
Race						
Caucasian	2.208	1.363–3.577	0.001	2.074	1.279–3.361	**0.003**
Black	0.672	0.380–1.186	0.170	0.501	0.283–0.887	**0.018**
Other	Reference			Reference		
Primary site						
prostate	Reference					
testis	1.329	0.185–9.548	0.777			
AJCC stage						
I	Reference					
II	0.878	0.281–2.744	0.822			
III	0.842	0.259–2.736	0.775			
IV	0.385	0.120–1.235	0.109			
Surgery						
Yes	Reference			Reference		
NO/Unknown	1.716	1.476–1.994	<0.001	1.405	1.187–1.664	**<0.001**
Radiation						
Yes	Reference			Reference		
NO/Unknown	0.806	0.689–0.943	0.007	0.933	0.780–1.115	0.443
Years elapsed from diagnosis						
<1	1.575	1.040–2.384	0.032	1.761	1.157–2.680	**0.008**
1	0.945	0.637–1.402	0.779	1.019	0.685–1.516	0.928
2	1.067	0.722–1.576	0.746	1.146	0.774–1.697	0.495
3	1.148	0.776–1.699	0.489	1.241	0.838–1.840	0.281
4	1.009	0.674–1.511	0.964	1.080	0.720–1.619	0.710
5	1.006	0.667–1.516	0.977	1.072	0.711–1.618	0.740
6	0.790	0.509–1.225	0.292	0.841	0.542–1.306	0.441
7	0.782	0.497–1.231	0.288	0.812	0.515–1.279	0.369
8	0.993	0.634–1.556	0.976	1.042	0.665–1.635	0.856
9	0.872	0.530–1.433	0.588	0.903	0.549–1.485	0.687
≥10	Reference			Reference		

Abbreviations: DSW, divorced & separated & widowed; AJCC stage, American Joint Committee on Cancer (AJCC) staging; 95%CI = 95% confidence interval. OR = odds ratio.

Table 3
Univariate and multivariate logistic regression analysis from 2010 to 2015.

Variables	Univariate analysis			Multivariate analysis		
	OR	95%CI	*P*-value	OR	95%CI	*P*-value
Age at diagnosis						
18–58	4.076	2.781–5.974	<0.001	4.613	3.136–6.784	**<0.001**
59–69	1.596	1.116–2.282	0.010	1.729	1.208–2.475	**0.003**
≥70	Reference	Reference				
Marital status						
Married	Reference					
Unmarried	0.999	0.645–1.546	0.995			
DSW	0.867	0.587–1.283	0.476			
Race						
Caucasian	8.751	1.233–62.601	0.031	8.399	1.173–60.123	**0.034**
Black	2.688	0.347–20.855	0.344	2.167	0.279–16.850	0.460
Other	Reference	Reference				
Primary site						
prostate	Reference					
testis			0.998			
AJCC stage						
I	Reference					
II			0.997			
III			0.997			
IV			0.997			
Surgery						
Yes	Reference	Reference				
NO/Unknown	1.719	1.266–2.335	0.001	1.553	1.141–2.113	**0.005**
Radiation						
Yes	Reference					
NO/Unknown	0.873	0.622–1.225	0.432			
Insurance status						
Insured	Reference					
Uninsured	0.249	0.035–1.785	0.167			
Any medicaid	0.538	0.274–1.055	0.071			
Years elapsed from diagnosis						
<1	1.347	0.181–10.034	0.771			
1	1.035	0.141–7.595	0.973			
2	1.209	0.165–8.871	0.852			
3	1.218	0.165–9.013	0.847			
4	1.485	0.200–11.046	0.699			
5	1.150	0.146–9.057	0.894			
6	Reference					

Abbreviations: DSW, divorced & separated & widowed; AJCC stage, American Joint Committee on Cancer (AJCC) staging; 95%CI = 95% confidence interval. OR = odds ratio.

patients might also be more representative of contemporary patient demographics. We therefore conducted a subgroup analysis of data from 2010 onwards. The age at diagnosis was also divided into 18–58, 59–69, and ≥70 years using the X-tile software (Fig. 3B). In univariate analysis, age, race, and surgery status were associated with suicide death. Multivariate logistic regression showed that age (18–58 vs ≥ 70 years: OR = 4.613, 95% CI = 3.136–6.784, $P < 0.001$; 59–69 vs ≥ 70 years: OR = 1.729, 95% CI = 1.208–2.475, $P = 0.003$), race caucasian(vs another race: OR = 8.399, 95% CI = 1.173–60.123, $P = 0.034$), and surgery (no/unknown vs yes: OR = 1.553, 95% CI = 1.141–2.113, $P = 0.005$) significantly increased the risk of suicide death. A time of <1 year after the diagnosis did not have a significant effect (Table 3).

Risk factors for suicide death according to AJCC staging systems

To explore how different risk factors in different American Joint Committee on Cancer (AJCC) staging systems affected suicide death in patients, we performed a stratified analysis of AJCC staging systems. For the 6th edition of the AJCC staging, no risk factors were found in stage I. In AJCC stage II, age (18–66 vs ≥ 76 years: OR = 4.104, 95% CI = 3.301–5.102, $P < 0.001$; 67–75 vs ≥ 76 years: OR = 2.039, 95% CI = 1.624–2.560, $P < 0.001$), marital status (unmarried vs married: OR = 1.308, 95% CI = 1.023–1.668, $P = 0.030$; DSW vs married: OR = 1.365, 95% CI = 1.121–1.661, $P = 0.002$), race caucasian (vs another race: OR = 2.811, 95% CI = 1.501–5.263, $P = 0.001$), and surgery (no/unknown vs yes: OR = 1.214, 95% CI = 1.000–1.473, $P = 0.050$) significantly increased the risk of suicide death. A time of <1 year after the diagnosis was also related to an increased risk of suicide death (<1 vs ≥ 10 years: OR = 2.024, 95% CI = 1.301–3.150, $P = 0.002$). In AJCC stage III, age (18–66 vs ≥ 76 years: OR = 4.084, 95% CI = 1.170–14.248, $P = 0.027$) was a risk factor. In AJCC stage IV, marital status (unmarried vs married: OR = 2.015, 95% CI = 1.062–3.825, $P = 0.032$) and surgery (no/unknown vs yes: OR = 2.283, 95% CI = 1.349–3.865, $P = 0.002$) were risk factors for suicide death.

We also performed a multivariate logistic regression analysis for the 7th edition of the AJCC staging. As indicated in Table 4, age (18–66 vs ≥ 76 years, OR = 8.551, 95% CI = 5.554–13.167, $P < 0.001$; 67–75 vs ≥ 76 years, OR = 1.911, 95% CI = 1.267–2.884, $P = 0.002$) was the only risk factor for AJCC stage II.

Discussion

Suicide is a major public health problem and male cancer patients have a higher risk of suicide [12,22]. According to our understanding, most studies have focused on the risk of suicide in patients with prostate cancer. However, there are few reports on the association of prostate cancer with suicide risk. In addition, there has been only one report on the risk of suicide in penile

Table 4
Multivariate logistic regression analysis in AJCC stage.

	The 6th edition of the AJCC stage for 2004–2015								
	II			III			IV		
Variables	OR	95%CI	*P*-value	OR	95%CI	*P*-value	OR	95%CI	*P*-value
Age at diagnosis							…		
18–66	4.104	3.301–5.102	**<0.001**	4.084	1.170–14.248	**0.027**			
67–75	2.039	1.624–2.560	**<0.001**	2.134	0.574–7.924	0.258			
≥76	Reference			Reference					
Marital status				…					
Married	Reference						Reference		
Unmarried	1.308	1.023–1.668	**0.030**				2.015	1.062–3.825	**0.032**
DSW	1.365	1.121–1.661	**0.002**				1.005	0.506–1.996	0.989
Race				…					
Caucasian	2.811	1.501–5.263	**0.001**				0.923	0.332–2.564	0.877
Black	0.696	0.345–1.406	0.313				0.201	0.044–0.914	**0.038**
Other	Reference						Reference		
Primary site	…			…			…		
prostate									
testis									
Surgery				…					
Yes	Reference						Reference		
NO/Unknown	1.214	1.000–1.473	**0.050**				2.283	1.349–3.865	**0.002**
Radiation	…			…			…		
Yes									
NO/Unknown									
Years elapsed from diagnosis				…			…		
<1	2.024	1.301–3.150	**0.002**						
1	1.224	0.808–1.854	0.340						
2	1.289	0.858–1.937	0.221						
3	1.269	0.844–1.909	0.253						
4	1.020	0.669–1.556	0.925						
5	1.113	0.731–1.696	0.617						
6	0.832	0.528–1.311	0.428						
7	0.749	0.466–1.204	0.233						
8	1.009	0.636–1.601	0.969						
9	0.868	0.520–1.447	0.586						
≥10	Reference								
The 7th edition of the AJCC stage for 2010–2015									
	II			III			IV		
Variables	OR	95%CI	*P*-value	OR	95%CI	*P*-value	OR	95%CI	*P*-value
Age at diagnosis				…			…		
18–58	8.551	5.554–13.167	**<0.001**						
59–69	1.911	1.267–2.884	**0.002**						
≥70	Reference								

Abbreviations: DSW, divorced & separated & widowed.; AJCC stage, American Joint Committee on Cancer (AJCC) staging; 95%CI = 95% confidence interval. OR = odds ratio.

cancer [18], and only one report on the risk of suicide in testicular cancer [23]. The present study is therefore the first to use the SEER database to investigate the burden of suicide death in MGSC patients in the United States.

Risk factors associated with suicide in the general population include chronic diseases, either being older or a youth, living alone, pain, and depression [12]. A meta-analysis found that prostate-cancer patients aged 75 years or older had an increased risk of suicide [24]. Another study found that patients <70 years old (SMR = 1.9, 95% CI = 1.4–2.6) had an increased risk of suicide after being diagnosed with prostate cancer [25]. Alanee et al. found that the standardized mortality ratio for suicide was 1.5 (95% CI = 1.1–2.1) among patients younger than 30 years with testicular cancer [23].

The present study use X-tile software to identify the best cutoffs for stratifying age. Using the SEER 2004–2015 data set, we found that age (18–66 vs ≥ 76 years: OR = 3.300, $P < 0.001$; 67–75 vs ≥ 76 years: OR = 1.832, $P < 0.001$) was independently associated with an increased risk of suicide death, with the risk being significantly higher in the youngest age group. Young and old cancer patients react differently to the impact of having cancer and undergoing treatment [26]. Anxiety and distress have been found to be less prevalent in older patients compared to younger patients [27]. Patients, especially young patients, should receive cancer-related mental risk education as soon as possible to make patients aware that the situation they encounter is not uncommon. They can safely communicate with their families and medical patients to avoid suicide due to patients' psychological pressure, fear of parents and friends, fear of social discrimination and other reasons.

We also found that being unmarried (OR = 1.332, $P = 0.010$) and DSW (OR = 1.338, $P = 0.002$) were risk factors for suicide death compared with married patients. A study of the increased risk of suicide in men with prostate cancer in New South Wales found that men who were single, divorced, widowed, or separated were more likely to suicide than married men (relative risk = 4.18, 95% CI = 2.36–7.42) [28]. Having a regular sexual partner and normal sex life may be good for suicide prevention. These patients may be more willing to discuss suicidal ideation with their partners and are likely to seek help. However, we did not obtain this result in our 2010–2015 subgroup analysis, which might have been due to the smallness of the sample in this subset of patients. We also found that being caucasian (compared to another race) was a significant risk factor for suicide death and being black was a protective factor for suicide in the 2004–2015 cohort. These race-related findings

are consistent with those of some previous studies [25,29].

Patients in the 2004–2015 cohort who did not receive surgery had a 1.405-fold higher risk of suicide than those who had received surgery ($P < 0.001$), while the risk was 1.553-fold higher in the 2010–2015 cohort ($P = 0.005$). Previous studies have shown that receiving treatment can reduce the risk of mental health problems and the risk of suicide [29,30]. This may be due to the restoration of similar sexual function and satisfactory quality of life in patients undergoing surgery. Patients who have not undergone surgery are more likely to have adverse physical consequences, such as pain, physical and mental stress, and depression. These patient characteristics may need to be closely monitored.

A particularly important finding of the present study was that patients at <1 year after the diagnosis had an increased risk of suicide death (<1 vs ≥ 10 years: OR = 1.761, $P = 0.008$). Carlsson et al. found that 38 of prostate-cancer patients suicided within the first 6 months after their diagnosis, giving an incidence rate of 0.73/1000 person-years [31]. Another study found that the suicide risk reduced over time after the diagnosis compared with <1 year after the diagnosis [28]. Our study also found that the suicide risk was higher in patients with MGSC within <1 year after the diagnosis, and that this elevated risk may last for several years. Although the finding was not statistically significant, the OR values were >1 for five consecutive years after the diagnosis, suggesting an increased risk of suicide. It is important to recognize the risk of suicide in the years following diagnosis. Long-term sensible follow-up is necessary for patients who are anxious, have received or have not undergone surgery, and have a relapsed disease.

We further analyzed the risk factors for suicide in patients according to AJCC stage. These results suggest that doctors and family members should pay special attention to whether MGSC patients have suicidal thoughts or behaviors when they are in AJCC stage II, and take timely measures to reduce the risk of suicide. Lower stage cancer to improve the life treatment of patients through conservative treatment. Higher stage cancer may require surgery such as radical resection or radiotherapy. When discussing different treatment models with patients, the risks associated with various treatment options should be identified. For example, hormone therapy may be associated with prolonged health-related quality of life and psychological pain [32]. In addition, radiotherapy was found to be associated with an increased risk of depression compared with other treatments [33].

Patients, family members and medical professionals should be educated about MGSC related suicide risks, such as diagnosis, treatment, eating health, exercise, quitting smoking, etc., to help avoid suicidal behavior. Disease progression can be prevented and controlled by changing poor lifestyles. In addition, appropriate pharmacological and psychological counselling is available to treat patients who have developed anxiety and depression [34]. For patients who have undergone surgery or radiotherapy, health care workers should try to relieve or alleviate the physical pain and discomfort of the patient. It is necessary to carry out continuous observation and treatment for patients with suicidal ideation or behavior.

Limitations

This study was subject to some limitations. Firstly, while disability status, pain, anxiety, depression, and previous psychotherapy are associated with suicidal ideation [35,36], we could not obtain relevant data from our analysis of the SEER database. Secondly, because we used data from a database, the cause of death may have been biased by misclassification. Finally, our study was inherently limited by its retrospective design.

Conclusion

This study found that age, being unmarried, being DSW, and no/unknown surgery significantly increased the risk of suicide death. Importantly, a time of <1 year after the diagnosis was related to an increased risk of suicide death, which indicates the importance of identifying and treating people at risk of suicide as early as possible. The present results can help clinicians to understand suicidal patients and provide them with appropriate support. We still need to actively explore the most effective methods to reduce the incidence and mortality of suicide in MGSC patients and improve the quality of life of patients.

Ethical disclosure

All of the authors signed the “SEER Research Data Agreement” in order to protect the patients’ privacy, which is consistent with ethical principles.

Conflict of interest

The authors declare no potential conflicts of interest.

Acknowledgments

This study was supported by the National Social Science Foundation of China (No.16BGL183) and the Research Fund of Health Bureau of Xi’an (No.QFO1330).

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