CLINICAL RESEARCH

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Received: 2019.10.15 Accepted: 2019.12.16 Available online: 2020.01.22 Published: 2020.03.09		Incidence and Risk Factors for Suicide Death among Kaposi's Sarcoma Patients: A Surveillance, Epidemiology, and End Results Analysis				
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Corresponding Author: Source of support:			work Foundation of China (81790631, 81570512), the National Key Research I Natural Science Foundation of Zhejiang Province, China (LQ19H030007)			
	ackground: I/Methods:	the Surveillance, Epidemiology, and End Results (death of suicide in patients with Kaposi's sarcom We screened KS patients without human immun 2016, calculated the standardized mortality ratio eral population from 1980 to 2016, and identified	than the general population. Our research aimed to explore SEER) database to define incidence and quest risk factors for a (KS) in the United States (US). odeficiency virus status in the SEER database from 1980 to s of them by comparing the rates with those of the US gen- relevant suicide risk factors by univariable and multivariable			
Ca	Results: onclusions:	and 15.1 per 100 000 person-years, respectively, dence interval [CI], 6.28–9.21). The multivariate ratio [HR]: 0.43, 95% CI: 0.21–0.89, P =0.022), and 0.31, 95% CI: 0.14–0.66, P =0.002), and chemothe P =0.032) were protective factors for suicide among Clinicians and caregivers can apply our findings	to identify KS patients with high suicide risk characteristics			
MeSH	Keywords:	(white race, age of 18-44 years, non-chemothera treatment, and follow-up to reduce the suicide ra Risk Factors • Sarcoma, Kaposi • SEER Program				
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Incidence and Risk Factors for Suicide



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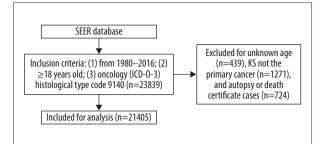
Background

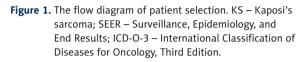
Suicide, one of the common causes of death in the United States (US) [1], is a complex behavior influenced by psychological, physiological, environmental, social, and cultural factors [2]. Previous studies have shown that people who were diagnosed with cancer may have increased risks of suicide ideas and attempt suicide [3–5], and patients with cancer and poor prognosis were more likely to feel desperate and depressed and subsequently committed suicide [4]. Several studies have shown that the rate of suicide in patients with cancer was nearly twice compared with that in the general population in the USA [6,7]. Another study revealed that the incidence of suicide was more than 3-fold higher in head and neck cancers patients than in the US general population [8].

Kaposi's sarcoma (KS) is an endothelial cell carcinoma that is etiologically linked to human herpes virus 8 (HHV-8) [9], which included 4 forms: 1) classic KS; 2) African KS; 3) AIDS-related KS; 4) iatrogenic KS. Classic KS is common among elderly Jewish, Mediterranean, and Middle Eastern human immunodeficiency virus (HIV)-negative men [10]. With the spread of AIDS epidemic, the KS incidence increased in 1980 and peaked in the late 1980s, becoming increasingly common in young patients with AIDS and weakened immune systems. However, after the antiretroviral therapy (ART) was widely used from 1996, the KS incidence dropped dramatically [11,12].

KS can cause skin lesions of purple, red, or brown spots, most often on the legs or face, but they can also develop in other parts of the body [13,14]. These skin lesions are very prominent and may attract attention from colleagues or passersby, which is a huge social and psychological burden for the patient. It has been suggested that KS-associated skin lesions can significantly affect quality of life [15,16], which may potentially increase risk of suicide in this group of patients. However, these is no dedicated study investigating the suicide incidence in patients with KS.

The National Cancer Institute's SEER program is a coordinated system of population-based state cancer registries that collects information on all cancer patients in representative geographical areas in the US [17], which includes 18 registries covering 30% of the US population [18]. Therefore, the SEER database may be used to explore the association between KS patients and the suicide behavior of them. Our study aimed to define the suicide rate and explore potential risk factors related with suicide in patients with KS by using SEER database.





Material and Methods

Patient selection

The SEER database provides registered researchers with information such as patient demographics, clinical data, and prognosis for free, but does not provide HIV status. We obtained a license to access the database after signing and submitting the SEER Research Data Agreement form. Then, we used SEER*Stat 8.3.4 to retrieve the data. Finally, we searched the patients with KS older than 18 years from the SEER database (1980–2016) by using the International Classification of Diseases for Oncology (ICD-O-3) histological type code 9140. All patients with KS were included, and 110 patients who died by suicide were identified. We excluded people for whom age was unknown, people for whom KS was diagnosed by autopsy or death certificate and people for whom KS was not the primary cancer. We identified 21 405 eligible patients in the database (Figure 1).

Covariates

We collected the information of interest about KS patients, including gender (male, female), the year of diagnosis, age at diagnosis (18-44, 45-54, ≥55 years old), race (black, white, other, unknown), marital status (married; single; divorced, separated or widowed [DSW]; unknown), tumor risk classification, surgery (yes, no, unknown), radiotherapy (yes, no, unknown), and chemotherapy (yes, no/unknown) by using the SEER*Stat software. We used the AIDS Clinical Trial Group (ACTG) staging criteria to classify the risk of tumor. To indicated that patients had low tumor risk and had single or multiple skin lesions. T, indicated that patients were considered to have a high risk of tumor, with single or multiple lesions in the mucosal tissue (e.g., mouth, anus, vagina, and others) or internal organs (e.g., lung, gastrointestinal tract, spleen, and others). T_{uk} indicated that the risk of tumor was unknown in patients with multiple lesions in nonspecific sites or unknown number and location of the tumor [10].

Statistical analysis

We used SPSS (version 22.0) software for the statistical analyses. By dividing the number of suicides in each category subset by the cumulative total survival time (in person year) of patients in that subset, the suicide rate per 100 000 personyears can be calculated. We calculated standardized mortality ratios (SMRs) with 95% confidence intervals (CIs) by determining the rate of suicides in the KS patients to suicides in the US general population. The total and subgroup rates of KS patients were compared with those of the US general population. Additionally, we divided patients into the following groups: death for suicide and death for other causes. We used the χ^2 -test to assess the differences in the patient features between these 2 groups. Logistic regression analysis was used to determine independent risk factors for suicide death. Only the variables with a P value <0.1 in the univariate logistic regression models were analyzed in multivariate logistic regression models. P<0.05 was considered statistically significant.

Results

Patient baseline characteristics

Overall, we identified 21 405 patients with KS from the SEER database from 1980–2016. Among them, 110 patients died of suicide, 15 429 patients died of other reasons, and 5866 patients were alive. Of those, 16 750 patients (78.3%) were white, and 3483 patients (16.3%) were black. Single was the predominant marital status. A total of 3793 patients (17.7%) underwent surgery, 4055 patients (18.9%) received radiotherapy, and 15 709 patients (73.4%) did not receive chemotherapy. All individuals who died by suicide were male. Regarding race, 99 patients (90.0%) were white, and 8 patients (7.3%) were black. Similarly, single was the predominant marital status. There were 15 patients (13.6%) who underwent surgery, 21 patients (19.1%) received radiotherapy, and 22 patients (20.0%) received chemotherapy. The patient demographic characteristics are summarized in Table 1.

Patient suicide incidence

From 1980 to 2016, 110 of 21 405 KS patients committed suicide for an observed 95 397 person-years, and the incidence of suicide was 115.31 per 100 000 person-years. The age-, sex-, and race-adjusted suicide rate in US general population during the corresponding period was 15.1. The standardized mortality ratio (SMR) of KS patients was 7.64 (95% CI, 6.28–9.21; P<0.001). Males (SMR, 4.85; 95% CI, 3.99–5.85; P<0.001), single individuals (SMR, 9.45; 95% CI, 7.59–11.63; P<0.001) and DSW individuals (SMR, 8.35; 95% CI, 3.57–16.53; P<0.001) had higher suicide rates than corresponding US general population. Age at diagnosis, race, treatment method, and tumor risk classification were not associated with increased suicide incidence (Table 2).

In terms of time periods, we discovered that the SMR of patients with KS remained at approximately 10–20 from 1980–1995; however, the first significant decrease in the SMR (1.98, 95% CI: 0.37–5.88) occurred from 1996–1997. Since then, SMR in patients with KS has generally declined despite fluctuations (Figure 2).

Factors associated with suicide

The univariable analysis results showed that advanced age at diagnosis (\geq 55 versus 18–44, HR: 0.53, 95% CI: 0.26–1.10, P=0.089), black race (versus white race, HR: 0.43, 95% CI: 0.21–0.89, P=0.023), chemotherapy (versus no chemotherapy, HR: 0.634, 95% CI: 0.40–1.01, P=0.056) and early diagnosis were associated with low risks of suicide. According to the multivariate analysis, black race (versus white race, HR: 0.43, 95% CI: 0.21–0.89, P=0.022), advanced age at diagnosis (\geq 55 versus 18–44, HR: 0.31, 95% CI: 0.14–0.66, P=0.002), chemotherapy (versus no chemotherapy, HR: 0.60, 95% CI: 0.37–0.96, P=0.032) and surviving 2 years after the diagnosis were protective factors. Conversely, apparent associations of sex, marital status, tumor risk classification, surgery, and radiotherapy were not found in KS patients (Table 3).

Discussion

Higher suicide risks in cancer populations had been verified by previous studies from different countries [7,19,20]. In the US, the rate of suicide in the general population is only half of that in cancer patients [6,7]. In addition, HIV-infection is associated with increased morbidity and risks of depression, also leading to higher risk of suicide than the general population [21]. It has been shown that classic KS accounts for over 90% in patients aged > 60 years or older [22,23]. In our study, 15% of the patients were diagnosed with KS at an age > 55 years, suggesting that classic KS only account for a small proportion of our patients. Therefore, we conclude that most KS cases in our study were caused by HIV infection despite that our study lacks the HIV status. According to our study, the suicide rate in KS patients was 115.31 per 100 000 person-years, and the SMR was 7.64 (95% CI, 6.28-9.21), indicating that the suicide risk was clearly increased compared with the US general population, which is 16.7/100 000 person-years [7].

We compared the rate of suicide in patients with KS and the US general population and defined which factors were related to a higher suicide incidence. Our research revealed that all individuals who died by suicide were male, the suicide rate of
 Table 1. Baseline characteristics of Kaposi's sarcoma patients.

Variables	Overall N (%) 21405		Nonsuicidal death N (%) 15429		Suicide death N (%) 110		Alive N (%) 5866	
Patients								
Marital status								
Married	2019	(9.4%)	1255	(8.1%)	5	(4.5%)	759	(12.9%)
Single	15 440	(72.1%)	11 768	(76.3%)	89	(80.9%)	3583	(61.1%)
DSW [#]	1563	(7.3%)	1202	(7.8%)	8	(7.3%)	353	(6.0%)
Unknown	2383	(11.1%)	1204	(7.8%)	8	(7.3%)	1171	(20.0%)
Sex								
Male	20 420	(95.4%)	14 800	(95.9%)	110	(100.0%)	5510	(93.9%)
Female	985	(4.6%)	629	(4.1%)	0	(0.0%)	356	(6.1%)
Race								
White	16 750	(78.3%)	12 547	(81.3%)	99	(90.0%)	4104	(70.0%)
Black	3483	(16.3%)	2347	(15.2%)	8	(7.3%)	1128	(19.2%)
Other	697	(3.3%)	457	(3.0%)	2	(1.8%)	238	(4.1%)
Unknown	475	(2.2%)	78	(0.5%)	1	(0.9%)	396	(6.8%)
Tumor risk classification##								
T _o	7859	(36.7%)	4972	(32.2%)	36	(32.7%)	2851	(48.6%)
T ₁	5538	(25.9%)	4213	(27.3%)	24	(21.8%)	1301	(22.2%)
T _{uk}	8008	(37.4%)	6244	(40.5%)	50	(45.5%)	1714	(29.2%)
Surgery								
Yes	3793	(17.7%)	2304	(14.9%)	15	(13.6%)	1474	(25.1%)
No	17 591	(82.2%)	13 117	(85.0%)	95	(86.4%)	4379	(74.7%)
Unknown	21	(0.1%)	8	(0.1%)	0	(0.0%)	13	(0.2%)
Radiotherapy								
Yes	4055	(18.9%)	3358	(21.8%)	21	(19.1%)	676	(11.5%)
No	17 281	(80.7%)	12 032	(78.0%)	88	(80.0%)	5161	(88.0%)
Unknown	69	(0.3%)	39	(0.3%)	1	(0.9%)	29	(0.5%)
Chemotherapy								
Yes	5696	(26.6%)	4364	(28.3%)	22	(20.0%)	1310	(22.3%)
No/Unknown	15 709	(73.4%)	11 065	(71.7%)		(80.0%)	4556	(77.7%)
Age at diagnosis								
18–44	14 731	(68.8%)	11 149	(72.3%)	83	(75.5%)	3499	(59.6%)
45–54	3464	(16.2%)	2260	(14.6%)	19	(17.3%)	1185	(20.2%)
≥55		(15.0%)		(13.1%)	8	(7.3%)	1182	(20.2%)

* DSW – divorced, separated or widowed. ** T_0 – means the patients had good tumor risk; T_1 – means patients had poor tumor risk; T_{nk} – means the risk of tumor was unknown.

Table 2. Suicide rate among patients with Kaposi's sarcoma.

Variables	Suicide death	Person – years	Suicide rate	Р	SMR ^{###}	95% CI
Total	110	95 396.63	115.31	<0.001***	7.64	6.28–9.2
Marital status						
Married	5	12 752.08	39.21	0.09	2.60	0.82–6.1
Single	89	62392.67	142.64	<0.001***	9.45	7.59–11.6
DSW [#]	8	6345.83	126.07	<0.001***	8.35	3.57–16.53
Unknown	8	13 906.00	57.53	0.006**	3.81	1.63–7.5
Sex						
Male	110	90 322.67	121.79	<0.001***	4.85	3.99–5.8
Female	0	5073.96	0	-	-	-
Race						
White	99	74 811.92	132.33	<0.001***	8.02	6.52–9.7
Black	8	14 473.92	55.27	<0.001***	7.47	3.19–14.7
Other	2	3328.08	60.09	0.08	6.83	0.64–25.1
Unknown	_	-	_	-	_	_
Tumor risk classification##						
T _o	36	43 537.17	82.69	<0.001***	5.48	3.83–7.5
T ₁	24	19 810.67	121.15	<0.001***	8.02	5.13–11.9
T _{uk}	50	32 048.75	156.01	<0.001***	10.33	7.67–13.6
Surgery						
Yes	15	24 028.08	62.43	<0.001***	4.13	2.31–6.8
No	95	71 267.42	133.30	<0.001***	8.83	7.14–10.7
Unknown	0	101.13	0	_	_	_
Radiotherapy						
Yes	21	16 765.58	125.26	<0.001***	8.30	5.13-12.7
No	88	78 238.67	112.48	<0.001***	7.45	5.97–9.1
Unknown	1	392.29	254.91	0.13	16.88	0.007–96.
Chemotherapy						
Yes	22	22 209.58	99.06	<0.001***	6.56	4.11–9.9
No/Unknown	88	73 187.00	120.24	<0.001***	7.96	6.39–9.8
Age at diagnosis						
18–44	83	61 613.04	134.71	<0.001***	9.76	7.77–12.1
45–54	19	15 893.54	119.55	<0.001***	7.11	4.28–11.1
≥55	8	17 890.04	44.72	0.03	2.69	1.15–5.3

[#] DSW – divorced, separated or widowed. ^{##} T_0 – means the patients had good tumor risk; T_1 – means patients had poor tumor risk; T_{nk} – means the risk of tumor was unknown. ^{###} SMR – standardized mortality ratio: reference population (age-, sex-, and race-adjusted US general population from 1980 to 2016). ^{**} *P*<0.01; ^{***} *P*<0.001.

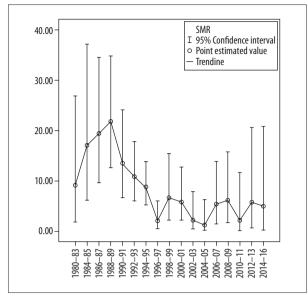


Figure 2. Standardized mortality ratio of suicide for Kaposi's sarcoma patients during 1980–2016.

them was 121.79 per 100 000 person-years, which is consistent with the results in other types of cancer patients [24,25]. The study by Kendal analyzed patients in the SEER registries during 1973-2001 and found the suicide HR for males was 6.2 [26]. Nock et al. [27] reported that women had a higher nonfatal self-injuries rate than men, but men had a higher suicide rate than women. This trend is often ascribed to the fact that men engage in more lethal and violent methods of suicide than women [28]. We also found that the suicide rates of singles (SMR=9.45, P<0.001) and DSW (SMR=8.35, P<0.001) individuals were higher than those of married individuals. Compared with unmarried individuals, married individuals generally have an increased cancer-specific survival rate and decreased mortality [29,30]. which could be because married individuals generally have better socioeconomic status and more social support than unmarried individuals [31-33]. Therefore, new treatment methods are often firstly used in the groups with better economic and social status, which may lead to a gap in the prognosis of the disease. With the development of medicine, new treatment methods have spread to people with a relatively low social and economic status, and the gap is expected to narrow. Therefore, this may partly explain that the SMR of married individuals is lower than that of unmarried individuals.

KS is different from other tumors (such as kidney cancer, liver cancer, lung cancer, etc.) in staging. The ACTG applied the extent of tumor (T), the severity of immunosuppression (I), and other HIV-related systemic diseases (S) to stage it. However, we only obtained data on the extent of tumor through the SEER database, and we cannot evaluate the other 2 indicators. In fact, the immune situation and other HIV-related systemic diseases had a significant effect on the prognosis of KS patients, so classifying the risk of tumor by the tumor extent will have a certain bias in results.

In our study, the change in the suicide rate in patients with KS over time should be noted. In Figure 2, the SMR peaked in the late 1980s, then declined from 1990, and reached its first trough in 1996-1997 (SMR: 1.98, 95% CI: 0.37-0.5.88). Since then, although SMR in patients with KS has fluctuated, it has generally declined compared with that before 1990. Previous studies have shown that since the introduction of antiretroviral therapy in early 1990, the efficacy of this treatment has gradually increased, thereby improving the immunity of KS patients with HIV infection and reducing the risk of them. From 1996, ART therapy has been used in most cases of KS [34,35]. The treatment of KS with ART has a certain effect on the survival rate, but long-term adherence is also necessary for successful treatment [36]. Moreover, chemotherapy or radiotherapy has been used as an adjuvant therapy for the treatment of patients with KS. Therefore, differences in treatment compliance may have led to the fluctuations in the SMR after 1996, especially the acceptance of radiotherapy and chemotherapy in patients. Unfortunately, we were unable to obtain information about sexual partners of KS patients, especially high-risk population related to the incidence of KS. Thus, we could not assess the impact of sexual partners on SMR of suicide in KS patients.

As shown in table of logistic regression analyses (Table 3), race is a factor associated with suicide. Previous studies have shown that the suicide rates of white and black races are 13 and 6 per 100 000 person-years, respectively [37]. Our research also shows that the black race had lower risk of suicide than the white race, which may be due to religious beliefs, support from family and the culture of refusal to commit suicide [38]. Another unpredicted finding is that the suicide risk in KS patients within the 2 years after diagnosis appears to be relatively lower, suggesting that a recent diagnosis could be a low risk factor for suicide. In contrast, a previous study found that the suicide risk after the diagnosis decreases over time [39]. In fact, the mortality rate of KS is high, thus considerable patients may die in the early stage of the disease and have no opportunity to commit suicide, which leads to the deviation of the statistical results and underestimation of suicide risk in the recently diagnosed patients.

In addition, we found that patients aged 55 years and older had a lower suicide rate than those aged 18 to 44 years. Cancer patients of different ages respond differently to cancer and treatments. Compared with young patients, the incidence of anxiety and pain in elderly patients is relatively low [40]. Young patients should receive psychological risk education of cancer-related suicide as early as possible to ensure that patients realize their thoughts and feelings are not uncommon. They can avoid

Table 3. Logistic regression analyses of patients with Kaposi's sarcoma.

Variables	Univar	iable analysis	Multiva	Multivariable analysis		
Variables	Р	HR (95% CI)	Р	HR (95% CI)		
Aarital status						
Married	Reference					
Single	0.16	1.90 (0.77–4.68)				
DSW [#]	0.37	1.67 (0.54–5.12)				
Unknown	0.37	1.67 (0.54–5.12)				
ex						
Male	Reference					
Female	0.99	0.00				
lace						
White	Reference		Reference			
Black	0.02*	0.43 (0.21–0.89)	0.02*	0.43 (0.21–0.89		
Other	0.41	0.55 (0.14–2.26)	0.51	0.63 (0.15–2.55		
Unknown	0.63	1.62 (0.22–11.80)	0.70	1.48 (0.20–10.88		
umor risk classification##						
T _o	Reference					
T ₁	0.36	0.79 (0.47–1.32)				
T _{uk}	0.65	1.11 (0.72–1.70)				
urgery						
Yes	0.70	0.90 (0.52–1.55)				
No	Reference					
Unknown	1.00	0.00				
adiotherapy						
Yes	0.52	0.86 (0.53–1.38)				
No	Reference					
Unknown	0.22	3.51 (0.48–25.80)				
hemotherapy						
Yes	0.06*	0.63 (0.40–1.01)	0.03*	0.60 (0.37–0.96		
No/Unknown	Reference		Reference			
ge at diagnosis						
18–44	Reference		Reference			
45–54	0.63	1.13 (0.68–1.86)	0.80	1.07 (0.64–1.77		
≥55	0.09*	0.53 (0.26–1.10)	0.002**	0.31 (0.14–0.66		

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Vedeblee	Univari	able analysis	Multivariable analysis		
Variables	Р	HR (95% CI)	Р	HR (95% CI)	
Years elapsed from diagnosis					
<1	0.001**	0.30 (0.15–0.61)	<0.001***	0.25 (0.12–0.50)	
<2	0.05*	0.49 (0.24–1.00)	0.01*	0.39 (0.19–0.80)	
<3	0.22	0.61 (0.28–1.35)	0.09	0.49 (0.22–1.11)	
<4	0.47	0.72 (0.29–1.79)	0.29	0.61 (0.24–1.53)	
<5	0.48	0.68 (0.24–1.98)	0.35	0.60 (0.21–1.74)	
<6	0.64	0.76 (0.24–2.41)	0.63	0.75 (0.24–2.39)	
<7	0.22	0.27 (0.04–2.14)	0.22	0.27 (0.04–2.14)	
<8	0.63	1.32 (0.42–4.20)	0.66	1.30 (0.41–4.14)	
<9	0.93	1.06 (0.29–3.83)	0.84	1.14 (0.31–4.14)	
<10	0.52	1.53 (0.42–5.56)	0.43	1.68 (0.46–6.14)	
≥10	Reference		Reference		

Table 3 continued. Logistic regression analyses of patients with Kaposi's sarcoma.

[#] DSW – divorced, separated or widowed. [#] T₀ – means the patients had good tumor risk; T₁ – means patients had poor tumor risk; T₁ – means the risk of tumor was unknown. * P<0.1; ** P<0.01; *** P<0.001.

suicide that is due to fear of discrimination by people and society, psychological stress and other reasons by communicating with their families and medical caregivers [41]. Chemotherapy is another influencing factor for suicide. In addition to ART as an essential treatment, combination with chemotherapy could further improve the prognosis of KS patients [35]. Unfortunately, we were unable to obtain information about specific chemotherapy drugs for patients with KS through the SEER database, so we could not analyze the impact of different chemotherapy regimens on suicide rates in the KS patients.

The suicide behavior of cancer patients is affected by various factors, especially psychosocial factors. Previous published studies have confirmed that patients with cancer have higher prevalence of depression than the general population, and severe depression have a nonnegligible effect on suicidal behavior. This is also true for patients with KS. Based on our findings, we recommend a psychiatric assessment of KS patients. At present, some tools can be used to identify the risk of depression, including the Beck Depression Scale [25]. Psychotherapy should be provided to cancer patients at risk of depression as soon as possible, which can reduce the suicide risk and improve the quality of life. Moreover, family member and social support for patients can help reduce the psychological burden of patients, thereby further preventing suicide.

There are some limitations to our research. The SEER database lacks information on social and economic status, sexual orientation, sexual partner, HIV status, and drug treatment (especially ART) of these patients, which may have important effects on suicidal behavior. In addition, the lack of data on suicide failure may lead to bias in the assessment of suicide risk. Besides, our study collected only cancer patient-related data in the US.

Conclusions

Our study explored independent risk factors for suicide in KS patients. Clinicians and caregivers can apply our findings to identify KS patients with high suicide risk characteristics (white race, age of 18–44 years, non-chemotherapy) and exert timely interventions during patient diagnosis, treatment, and follow-up to reduce the suicide rate in this population. Further analysis of KS patients with known HIV status is needed to understand the potential effect of HIV infection on suicide incidence.

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Conflict of interests

None.

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