Suicide among cancer patients: adolescents and young adult (AYA) versus all-age patients

Huaqiang Zhou[1,2,3,4#], Wei Xian[4#], Yaxiong Zhang[1,2,3#], Yunpeng Yang[1,2,3], Wenfeng Fang[1,2,3], Jiaqing Liu[4], Jiayi Shen[4], Zhonghan Zhang[1,2,3], Shaodong Hong[1,2,3], Yan Huang[1,2,3], Li Zhang[1,2,3]

[1]Department of Medical Oncology, Sun Yat-sen University Cancer Center, Guangzhou 510060, China; [2]State Key Laboratory of Oncology in South China, Guangzhou 510060, China; [3]Collaborative Innovation Center for Cancer Medicine, Guangzhou 510060, China; [4]Zhongshan School of Medicine, Sun Yat-sen University, Guangzhou 510080, China

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[#]These authors contributed equally to this work.

Correspondence to: Li Zhang. Department of Medical Oncology, Sun Yat-sen University Cancer Center, 651 Dongfeng Road East, Guangzhou 510060, China. Email: zhangli6@mail.sysu.edu.cn.

Background: Many researchers have studied suicide risk factors of patients with one specific cancer. But there is no comprehensive study to compare suicide issues between adolescents and young adult (AYA) group and all-age groups in a pan-cancer view.

Methods: Patients diagnosed with 20 solid malignancies were identified from SEER database. Multivariable logistic regression was operated to find out risk factors of suicide.

Results: Male sex has less impact on AYA than all-age patients (OR 2.72, 95% CI: 2.23–3.31, P<0.001 *vs.* OR 4.64, 95% CI: 4.37–4.94, P<0.001), while white race (OR 3.28, 95% CI: 2.02–5.77, P<0.001 *vs.* OR 3.40, 95% CI: 3.02–3.84, P<0.001) and unmarried status (OR 1.51, 95% CI: 1.24–1.83, P<0.001 *vs.* OR 1.39, 95% CI: 1.33–1.46, P<0.001) have similar impact on AYA and all-age groups. Localized cancer stage may have stronger impact on AYA than all-age (OR 2.90, 95% CI: 1.83–4.84; P<0.001 *vs.* OR 1.76, 95% CI: 1.61–1.92; P<0.001), while surgery only influence all-age (OR 1.14, P=0.451 *vs.* 1.24, P<0.001). Within 5 years from cancer diagnosis, longer survival time is associated with higher suicide risk of both all-age and AYA patients.

Conclusions: Male sex, white race and unmarried status, earlier cancer stage and longer survival time within 5 years are similar prevalent risk factors for both AYA group patients and all-age patients. It is not necessary to pick AYA cancer patients out when considering suicide risk of cancer patients.

Keywords: Suicide; adolescents and young adult (AYA); Surveillance, Epidemiology, and End Results (SEER); risk factors; prevention

Introduction

Suicide accounted for 1.4% of all deaths worldwide, making it one of leading cause of death in 2016 (1). Cancer patients in US have nearly twice the suicide rate of the general population (2). Researchers have demonstrated suicide risk factors of patients with one specific cancer, such as lung cancer, colorectal cancer, head and neck cancer and so on (3-7). It has been discovered that male sex, white race, and older age at diagnosis may be associated with higher risk of suicide among cancer patients (2).

Adolescents and young adults (AYA) are defined as people whose age is between 15 and 39 (8). In 2017, adolescents and young adults aged 15 to 24, 25 to 34, 35 to 44 had a

suicide rate of 14.46, 17.53, 17.94 per 100,000 individuals in US respectively (9). About 70,000 adolescence and young adult (ages 15–39) are diagnosed with cancer each year in the United States, and cancer is the leading cause of disease-related death in the AYA population (8). Additionally, cancer incidence increased faster in AYAs than in younger or older population (10). Nowadays, AYA cancer patients lose advantage of prognosis compared to older cancer patients, and survival quality of AYA cancer patients should be focused on (11).

However, there is no comprehensive study to compare suicide issues between AYA group and all-age group in pan-cancer view. The purpose of this research is to analyze the necessity to separate AYA cancer patients as a special group to identify high risk patients.

Methods

Eligible cancer survivors were identified from National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database. SEER is a publicly accessible source of cancer patient information in the United States. This database collects cancer incidence data from population-based cancer registries covering approximately 34.6 percent of the U.S. population diagnosed between 1973 and 2015 (12).

Data of patients diagnosed with 20 types of solid malignancies (tumors of the nasopharynx, esophagus, stomach, colon and rectum, liver, gallbladder, pancreas, lung and bronchus, bones, joints and soft tissue, melanoma, breast, cervix uteri, corpus and uterus, ovary, prostate, urinary bladder, kidney and renal pelvis, eye and orbit, brain and other nervous system, and thyroid) were obtained from SEER database (1973–2015) using the SEER*Stat software (v8.3.5, Cancer Statistic Branch, NCI, Calverton), using International Classification of Disease for Oncology, Third Edition (ICD-O-3), morphology codes (13). Patients with unknown follow-up or recorded by autopsy and death certificate were eliminated.

Inclusion of patients with multiple primary cancers may have potential effect on suicidal behaviors which may lead to different result of high-risk population (5,14). To prevent the interference of multiple primary cancers, we extracted data of patients diagnosed with only one primary cancer of 20 kinds of solid carcinoma. Demographic and clinicopathological variables of interest encompassed sex, race, marital status, age at diagnosis, year of diagnosis, grade, stage, surgery, cause of death and survival time.

Patients whose cause of death variable coded as "Suicide and self-inflicted injury" were identified. They were divided into 3 groups according to age at diagnosis (younger than 15 years, 15–39 years, and older than 40 years). We sorted patients by white, black and others, and categorized patients as married or unmarried. Year of diagnosis were allocated into 3 groups (before 1993, 1994–2003, after 2004). Surgery was classified as performed, not performed, and unknown. Disease stage for the analysis was coded based on the variable "SEER Historic Stage A". We give a value of 0.5 months to those who didn't survive for a full month after diagnosis, because SEER record their survival time in months (13).

To examine patients committed suicide with those died from other causes, univariate analysis using chi-square test was applied. We employed multivariable logistic regression to distinguish independent risk factors for suicide. All statistical analyses were performed using R version 3.4.2 software (Institute for Statistics and Mathematics, Vienna, Austria; www.r-project.org). Statistical significance was set at two-sided P<0.05.

Results

Patient cohort characteristics

We identified 5,261,459 patients, and 312,313 of them are AYA patients. The SMR for AYA is slightly lower than that for all identified patients (0.14%, 433 in 312,313 vs. 0.15%, 7,831 in 5,261,459, P=0.150) (Table S1). Highest SMR is seen in nasopharynx cancer (0.34% vs. 0.38%), prostate cancer (0.26% vs. 0.29%) and urinary bladder cancer (0.26% vs. 0.37%) when comparing AYA and all-age patients. Decrease of SMR is observed both in AYA group and all-age group cancer patients as time goes by (Tables S2,S3).

Risk factors of suicide in AYA group and all-age group cancer survivors

When analyzed in pan-cancer view, male sex, white race, unmarried status, earlier stage and later time from cancer diagnosis are suicide risk factors for both AYA and all-age cancer patients. The effect of gender on the AYA group was not as obvious as that of the whole age group when consider all cancers (OR 2.72, 95% CI: 2.23–3.31, P<0.001 vs. OR 4.64, 95% CI: 4.37–4.94, P<0.001) (Table 1). Race has similar effects on AYA patients and all-age patients (OR 3.28, 95% CI: 2.02–5.77, P<0.001 vs. OR 3.40, 95% CI:

Table 1 Odds ratio (OR) and its 95% confidence interval for increased suicide risk in AYA group and all-age group contributed by demographic factors, SEER, 1973–2015

Cancer type	Male sex[a]				White race[b]				Unmarried status[c]			
	All-age		AYA		All-age		AYA		All-age		AYA	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Nasopharynx	17.51	(3.79–311.36)	–	–	2.74	(0.81–17.19)	0.74	(0.13–5.81)	0.96	(0.47–1.86)	0.71	(0.15–3.30)
Esophagus	6.70	(3.35–15.91)	–	–	6.28	(3.48–20.59)	–	–	1.51	(1.23–2.11)	–	–
Stomach	5.42	(3.52–8.75)	1.27	(0.30–6.45)	5.43	(2.47–15.31)	–	–	1.13	(0.83–1.52)	1.12	(0.25–4.96)
Colon and rectum	5.97	(5.01–7.15)	3.07	(1.52–6.84)	4.03	(2.78–6.11)	2.29	(0.82–9.57)	1.43	(1.25–1.63)	1.48	(0.80–2.79)
Liver	7.84	(2.88–32.22)	–	–	1.16	(0.55–2.82)	–	–	0.98	(0.58–1.66)	–	–
Gallbladder	42.32	(8.12–777.85)	–	–	1.41	(0.27–26.01)	–	–	2.04	(0.68–6.09)	–	–
Pancreas	9.44	(5.66–16.92)	0.37	(0.00–13.81)	3.30	(1.58–8.44)	–	–	1.65	(1.17–2.32)	–	–
Lung	6.18	(5.15–7.46)	2.75	(0.81–12.55)	4.20	(3.07–5.94)	–	–	1.38	(1.22–1.55)	1.78	(0.56–6.12)
Bone	3.60	(1.75–8.39)	1.41	(0.51–4.51)	2.23	(0.68–13.73)	–	–	1.62	(0.82–3.27)	1.89	(0.65–6.84)
Melanoma	4.29	(3.38–5.51)	2.99	(1.92–4.76)	–	–	–	–	1.30	(1.08–1.56)	1.28	(0.84–1.97)
Breast	4.32	(2.64–6.64)	–	–	3.00	(2.05–4.60)	3.36	(1.36–11.14)	1.15	(0.98–1.34)	1.99	(1.22–3.26)
Cervix uteri	–	–	–	–	12.87	(2.83–227.75)	–	–	0.89	(0.56–1.42)	1.32	(0.69–2.53)
Uterus	–	–	–	–	4.78	(1.50–29.10)	0.99	(0.17–18.94)	0.95	(0.65–1.39)	1.98	(0.47–9.91)
Ovary	–	–	–	–	6.54	(1.44–115.59)	1.38	(0.26–25.49)	0.86	(0.55–1.34)	1.31	(0.41–4.50)
Prostate	–	–	–	–	3.10	(2.62–3.70)	0.99	(0.09–22.68)	1.46	(1.34–1.58)	3.08	(0.26–70.34)
Urinary bladder	7.12	(5.06–10.42)	3.32	(0.94–21.06)	2.67	(1.55–5.18)	0.62	(0.16–4.04)	1.32	(1.11–1.56)	1.05	(0.40–2.68)
Kidney and renal pelvis	4.35	(3.06–6.35)	1.50	(0.48–5.62)	3.73	(1.97–8.25)	–	–	1.97	(1.52–2.56)	4.40	(1.38–16.91)
Eye	2.87	(1.33–6.90)	2.51	(0.21–60.16)	–	–	–	–	0.84	(0.38–1.73)	1.61	(0.12–37.72)
Brain and other nervous system	3.69	(2.30–6.25)	2.32	(1.19–4.98)	1.96	(0.82–6.44)	3.94	(0.85–70.14)	1.31	(0.87–1.98)	1.22	(0.67–2.27)
Thyroid	4.44	(3.17–6.27)	4.19	(2.31–7.63)	4.90	(1.56–29.72)	–	–	1.68	(1.19–2.37)	1.34	(0.74–2.42)
Total	4.64	(4.37–4.94)	2.72	(2.23–3.31)	3.40	(3.02–3.84)	3.28	(2.02–5.77)	1.39	(1.33–1.46)	1.51	(1.24–1.83)

SEER, Surveillance, Epidemiology, and End Results; AYA, adolescence and young adult. [a]Female sex as reference; [b]Black race as reference; [c]Married status as reference.

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3.02–3.84, P<0.001) (*Table 1*). Impact of marital status on AYA patients and all-age patients are similar as well (OR 1.51, 95% CI: 1.24–1.83, P<0.001 *vs.* OR 1.39, 95% CI: 1.33–1.46, P<0.001) (*Table 1*). Localized stage of cancer is associated with higher risk of suicide in all-age patients, and the association is stronger in AYA patients (OR 1.76, 95% CI: 1.61–1.92, P<0.001 *vs.* OR 2.90, 95% CI: 1.83–4.84, P<0.001) (*Table 2*) Surgery is related to suicide in all-age cancer patients, but it don't have significant impact on suicide ideal in AYA cancer patients (OR 1.24, 95% CI: 1.17–1.31, P<0.001 *vs.* OR 1.14, 95% CI: 0.82–1.59, P=0.451) (*Table 2*). Within 5 years from cancer diagnosis, longer survival time is associated with higher suicide risk of both all-age and AYA patients (*Table 3*).

Suicide risk of specific cancer patients in AYA group and all-age group is affected by the same demographic factor differently. Compared to female patients, male patients with pancreas cancer are most likely to suicide in all ages (OR 9.44, 95% CI: 5.66–16.92, P<0.001) (*Table 1*), while male AYA patients with thyroid cancer have highest risk of suicide (OR 4.19, 95% CI: 2.31–7.63, P<0.001) (*Table 1*). When considering ethnicity of patients, white patients with esophagus cancer take higher risk of suicide (OR 6.28, 95% CI: 3.48–20.59, P<0.001) (*Table 1*) while white AYA patients with breast cancer (OR 3.36, 95% CI: 1.36–11.14, P=0.020) (*Table 1*) are most potential to commit suicide. As for unmarried patients, those with kidney and renal pelvis cancer are most likely to suicide both in AYA (OR 4.40, 95% CI: 1.38–16.91, P=0.017) (*Table 1*) and in all (OR 1.97, 95% CI: 1.52–2.56, P<0.001) (*Table 1*).

Clinicopathological factor also have different influence on suicide risk of specific cancer patients in AYA group and all-age group. When using distant stage as reference, localized stage has greatest impact on breast cancer patients both in all-age group (OR 5.16, 95% CI: 3.17–8.96, P<0.001) and AYA group (OR 7.55, 95% CI: 1.47–139.76, P=0.055) (*Table 2*). Compared to those didn't undergo surgery, brain and other nervous system cancer patients who undergo surgery have higher risk of suicide (OR 1.95, 95% CI: 1.21–3.31, P=0.009) (*Table 2*), and surgery don't have significant impact on specific type of cancer in AYA patients as well.

Suicide risk of specific cancer patients in AYA group and all-age group influenced by period from cancer diagnosis differently. At the first year of cancer diagnosis, all-age patients with breast cancer are most likely to suicide (OR 3.71, 95% CI: 2.92–4.67, P<0.001). While AYA patients with cervical cancer have highest

suicide risk (OR 5.11, 95% CI: 1.98–12.24, P<0.001) (*Table 3*). Ovarian cancer patients are most likely to suicide in all-age group (OR 2.65, 95% CI: 1.03–6.07, P=0.029) and kidney and renal pelvis cancer patients have highest suicide risk in AYA group (OR 15.22, 95% CI: 2.97–62.34, P<0.001) at the fifth year of cancer diagnosis.

Discussion

Our study observed that suicide rate of AYA cancer patients is marginally lower than all-age cancer patients. On one hand, AYA cancer patients may use internet more frequently than older patients or children (15,16). They may acquire more information about their cancer and psychological support from the Internet, which may enhance their confidence to fight against cancer and lower their ideal of suicide (15,17). On the other hand, AYA cancer patients may have need of fertility preservation, and it may provide AYA cancer patients the impetus to survive (18). According to the result, both AYA patients and all-age patients with nasopharynx cancer, prostate cancer and urinary bladder cancer have highest SMR. But former researches showed highest suicide rate occur in lung, stomach, and head and neck cancers patients, which is not completely consistent with our result (2). Also, the sites correlated with the greatest suicide rate vary depending on the report (3,19,20). The underlying reason is unknown, and it may be explained that nasopharynx cancer has a catastrophic impact on patients' quality of life (21,22). Contrary to increasing suicide rate of US population, significant improvement in suicide prevention is observed both in AYA group and all-age group cancer patients (23). This result is consistent with previous studies (20,24). It may be explained by the improvement of prognosis of all-age cancer patients and AYA cancer patients due to development of advanced therapy such as targeted chemotherapy and immunotherapy (10,25-28).

Clinical implications

Demographic factors of patients show close relationship with suicide risk of both AYA cancer patients. We discovered that male patients of both AYA group and all-age group patients are more likely to commit suicide, which is accordant with US general population (1). Previous studies also displayed that male sex is risk factor of suicide in many types of cancer patients (2,29). However, male sex has less impact on suicide risk of AYA cancer patients compared

Table 2 Odds ratio (OR) and its 95% confidence interval for increased suicide risk in AYA group and all-age group contributed by clinicopathological factors, SEER, 1973–2015

Cancer type	Stage	Tumor stage[a]				Surgery[b]			
		All-age		AYA		All-age		AYA	
		OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Nasopharynx	Localized	3.37	(0.63–25.03)	–	–	0.99	(0.39–2.16)	0.54	(0.03–3.48)
	Regional	2.88	(0.81–18.42)	1.66	(0.23–35.09)				
Esophagus	Localized	1.54	(0.93–2.54)	–	–	1.02	(0.67–1.31)	–	–
	Regional	1.73	(1.47–1.96)	–	–				
Stomach	Localized	1.62	(1.04–2.49)	2.53	(0.24–21.81)	1.04	(0.73–1.48)	1.44	(0.23–8.06)
	Regional	1.04	(0.68–1.59)	0.73	(0.03–7.49)				
Colon and rectum	Localized	2.34	(1.87–2.95)	4.25	(1.36–16.21)	0.90	(0.72–1.15)	1.03	(0.36–3.47)
	Regional	2.07	(1.66–2.60)	4.49	(1.6–16.11)				
Liver	Localized	1.62	(0.76–3.76)	–	–	1.28	(0.65–2.40)	–	–
	Regional	0.92	(0.38–2.27)	–	–				
Gallbladder	Localized	0.54	(0.09–2.67)	–	–	2.00	(0.57–8.09)	–	–
	Regional	1.00	(0.27–3.51)	–	–				
Pancreas	Localized	0.99	(0.50–1.79)	12.22	(0.27–691.59)	1.08	(0.62–1.80)	0.74	(0.01–40.38)
	Regional	0.89	(0.56–1.36)	–	–				
Lung	Localized	1.33	(1.08–1.64)	0.41	(0.02–5.51)	1.47	(1.26–1.71)	2.40	(0.57–11.29)
	Regional	1.18	(0.99–1.40)	1.63	(0.22–14.54)				
Bone	Localized	4.28	(1.49–14.40)	3.41	(0.62–64.54)	1.25	(0.60–2.70)	0.95	(0.29–3.67)
	Regional	3.29	(1.13–11.08)	2.74	(0.44–53.57)				
Melanoma	Localized	2.55	(1.44–4.91)	–	–	1.21	(0.78–1.95)	0.85	(0.33–2.94)
	Regional	2.37	(1.29–4.68)	–	–				
Breast	Localized	5.16	(3.17–8.96)	7.55	(1.47–139.76)	1.16	(0.80–1.71)	1.20	(0.32–8.02)
	Regional	4.41	(2.70–7.66)	3.83	(0.73–71.31)				
Cervix uteri	Localized	4.05	(1.32–17.74)	6.95	(1.29–129.59)	1.05	(0.58–1.94)	0.49	(0.23–1.11)
	Regional	1.74	(0.56–7.61)	2.07	(0.34–39.38)				
Uterus	Localized	2.62	(1.17–7.01)	–	–	1.62	(0.78–3.78)	–	–
	Regional	2.83	(1.18–7.87)	–	–				
Ovary	Localized	2.30	(1.28–4.08)	3.56	(0.81–26.16)	0.78	(0.41–1.54)	0.37	(0.04–8.72)
	Regional	1.70	(0.69–3.60)	–	–				
Prostate	Localized/regional	1.49	(1.19–1.89)	–	–	1.05	(0.97–1.14)	1.31	(0.10–34.88)
Urinary bladder	Localized	4.40	(2.21–10.41)	–	–	1.17	(0.81–1.76)	–	–
	Regional	4.39	(2.19–10.42)	–	–				

Table 2 (*continued*)

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Table 2 (*continued*)

Cancer type	Stage	Tumor stage[a]				Surgery[b]			
		All-age		AYA		All-age		AYA	
		OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Kidney and renal pelvis	Localized	1.90	(1.24–2.96)	2.02	(0.29–41.85)	1.12	(0.74–1.73)	–	–
	Regional	1.10	(0.67–1.80)	–	–				
Eye	Localized	0.62	(0.12–11.50)	–	–	0.83	(0.39–1.74)	–	–
	Regional	1.17	(0.15–24.10)	–	–				
Brain and other nervous system	Localized	–	–	–	–	1.95	(1.21–3.31)	1.87	(0.86–4.70)
	Regional	–	–	–	–				
Thyroid	Localized	1.23	(0.66–2.47)	0.50	(0.19–1.71)	1.32	(0.64–2.96)	–	–
	Regional	0.89	(0.47–1.79)	0.39	(0.14–1.37)				
Total	Localized	1.76	(1.61–1.92)	2.90	(1.83–4.84)	1.24	(1.17–1.31)	1.14	(0.82–1.59)
	Regional	1.46	(1.33–1.59)	1.98	(1.23–3.35)				

SEER, Surveillance, Epidemiology, and End Results; AYA, adolescence and young adult. [a]Distant tumor stage as reference; [b]Not undergoing surgery as reference.

Table 3 Odds ratio (OR) and its 95% confidence interval for increased suicide risk in AYA group and all-age group contributed by time from cancer diagnosis, SEER, 1973–2015

Cancer type	1 year[a]		2 years[a]		3 years[a]		4 years[a]		5 years[a]	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
All-age										
Nasopharynx	1.23	(0.56–2.67)	0.66	(0.19–1.79)	0.25	(0.01–1.24)	1.77	(0.58–4.56)	–	–
Esophagus	1.75	(0.87–4.06)	0.98	(0.58–2.48)	1.10	(0.38–2.03)	0.90	(0.38–3.14)	2.96	(0.97–8.55)
Stomach	1.68	(1.02–2.88)	1.98	(1.13–3.54)	1.00	(0.41–2.20)	2.71	(1.31–5.39)	1.43	(0.48–3.52)
Colon and rectum	1.25	(1.03–1.51)	1.56	(1.27–1.91)	1.65	(1.32–2.05)	1.33	(1.01–1.71)	1.46	(1.10–1.91)
Liver	1.46	(0.48–6.39)	3.05	(0.96–13.52)	1.74	(0.38–8.98)	1.47	(0.19–8.98)	3.25	(0.60–17.73)
Gallbladder	0.81	(0.12–16.47)	–	–	2.46	(0.22–54.73)	–	–	–	–
Pancreas	1.27	(0.45–5.32)	1.39	(0.45–6.03)	2.17	(0.62–9.95)	1.17	(0.15–7.12)	–	–
Lung	1.07	(0.85–1.35)	1.07	(0.83–1.38)	0.90	(0.65–1.24)	1.09	(0.74–1.56)	1.27	(0.84–1.88)
Bone	2.82	(1.28–6.14)	2.04	(0.77–4.88)	–	–	2.90	(0.93–7.64)	2.03	(0.47–6.24)
Melanoma	2.10	(1.56–2.80)	1.71	(1.22–2.35)	1.75	(1.22–2.44)	2.13	(1.50–2.96)	2.32	(1.61–3.27)
Breast	3.71	(2.92–4.67)	2.77	(2.14–3.54)	2.55	(1.95–3.29)	2.03	(1.49–2.70)	2.04	(1.49–2.75)
Cervix uteri	2.20	(1.05–4.40)	2.38	(1.07–4.87)	1.45	(0.43–3.73)	1.50	(0.36–4.26)	2.43	(0.71–6.25)
Uterus	3.17	(1.80–5.42)	2.04	(1.17–3.87)	2.06	(0.93–4.05)	0.55	(0.09–1.80)	2.56	(1.11–5.19)
Ovary	1.40	(0.69–2.80)	1.72	(0.80–3.57)	1.65	(0.67–3.70)	2.28	(0.92–5.09)	2.65	(1.03–6.07)

Table 3 (*continued*)

Table 3 (*continued*)

Cancer type	1 year[a]		2 years[a]		3 years[a]		4 years[a]		5 years[a]	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Prostate	2.16	(1.91–2.44)	1.97	(1.72–2.26)	1.76	(1.52–2.03)	2.02	(1.75–2.32)	1.58	(1.35–1.84)
Urinary bladder	1.68	(1.33–2.10)	1.20	(0.90–1.59)	1.58	(1.18–2.09)	1.33	(0.95–1.83)	1.43	(1.00–1.98)
Kidney and renal pelvis	1.37	(0.91–2.04)	2.51	(1.68–3.7)	1.56	(0.92–2.54)	1.57	(0.89–2.62)	2.52	(1.53–3.99)
Eye	0.64	(0.10–2.42)	2.94	(1.08–7.33)	1.94	(0.54–5.55)	1.02	(0.16–3.75)	2.67	(0.74–7.66)
Brain and other nervous system	0.61	(0.36–1.03)	0.61	(0.31–1.14)	0.41	(0.12–1.03)	0.80	(0.27–1.88)	1.02	(0.35–2.38)
Thyroid	2.83	(1.61–4.83)	3.59	(1.86–6.54)	3.51	(1.73–6.60)	2.14	(0.86–4.53)	2.63	(1.13–5.39)
Total	1.33	(1.24–1.42)	1.53	(1.42–1.65)	1.53	(1.40–1.67)	1.63	(1.48–1.78)	1.59	(1.44–1.75)
AYA										
Nasopharynx	4.41	(0.49–39.42)	5.93	(0.67–52.6)	–	–	11.04	(1.22–101.96)	–	–
Esophagus	–	–	–	–	–	–	–	–	–	–
Stomach	4.04	(0.45–88.43)	–	–	–	–	17.03	(1.51–386.62)	–	–
Colon and rectum	2.34	(0.85–6.05)	3.36	(1.27–8.43)	3.68	(1.25–9.75)	2.49	(0.56–8.00)	5.56	(1.73–15.34)
Liver	–	–	–	–	–	–	–	–	–	–
Gallbladder	–	–	–	–	–	–	–	–	–	–
Pancreas	–	–	–	–	–	–	–	–	–	–
Lung	0.39	(0.08–1.78)	–	–	–	–	2.72	(0.38–12.67)	–	–
Bone	1.70	(0.25–7.26)	0.85	(0.04–4.81)	–	–	7.57	(1.86–26.63)	4.14	(0.60–17.69)
Melanoma	1.14	(0.32–2.98)	1.00	(0.24–2.81)	1.18	(0.28–3.27)	3.18	(1.30–6.68)	4.13	(1.77–8.42)
Breast	2.26	(0.80–5.38)	0.80	(0.19–2.27)	1.69	(0.63–3.78)	0.95	(0.23–2.67)	2.30	(0.86–5.16)
Cervix uteri	5.11	(1.98–12.24)	2.13	(0.48–6.66)	4.40	(1.23–12.32)	3.15	(0.49–11.41)	2.08	(0.11–10.54)
Uterus	–	–	7.95	(0.35–72.17)	22.47	(2.30–160.60)	–	–	10.94	(0.47–99.63)
Ovary	0.74	(0.04–5.04)	–	–	1.71	(0.09–10.73)	2.14	(0.11–14.03)	–	–
Prostate	2.31	(0.09–29.66)	–	–	–	–	–	–	–	–
Urinary bladder	2.82	(0.14–17.58)	–	–	5.76	(0.29–37.43)	9.90	(1.38–43.62)	14.61	(2.92–55.40)
Kidney and renal pelvis	–	–	3.35	(0.16–22.36)	–	–	10.77	(1.39–54.95)	15.22	(2.97–62.34)
Eye	–	–	–	–	49.64	(2.90–1,700.04)	–	–	–	–
Brain and other nervous system	0.69	(0.27–1.59)	1.34	(0.56–2.91)	–	–	0.71	(0.11–2.43)	1.56	(0.45–4.14)
Thyroid	1.76	(0.26–6.85)	3.64	(0.79–12.09)	4.32	(0.92–14.76)	2.98	(0.44–11.94)	–	–
AYA total	1.26	(0.89–1.76)	1.40	(0.94–2.02)	1.70	(1.12–2.49)	2.58	(1.76–3.68)	2.82	(1.90–4.05)

SEER, Surveillance, Epidemiology, and End Results; AYA, adolescence and young adult. [a]Time form cancer diagnosis ≥6 years as reference.

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to all-age patients. AYA cancer patients may suffer from harder financial situation than other patients, and male patients may be the breadwinner of his family (30). Thus, male AYA patients would rather struggle to live than ending their live. Another possible reason is that female AYA patients may have higher suicidal thoughts than other age patients (31). White patients also have higher risk of committing suicide, and race has a similar impact on suicidal ideation of AYA and all-age group. Former research discovered that black and white did not significantly differ in frequency of psychiatric conditions in suicide patients in Michigan HealthCare System (32). The reason for higher suicide risk in white patients in all-age group and AYA group remains unknown, and hopelessness may be associated with higher suicide risk in white patients (33). Unmarried status is also relative with greater suicide risk of AYA and all-age cancer patients. Impact of marital status on suicide risk of AYA group and all-age group is alike. A recent review has shown that both objective social isolation and the subjective feeling of loneliness due to unmarried status can explain higher suicide risk in AYA and older patients (34).

Interestingly, when analyze suicide risk in specific cancer patients, male sex and white race and marital status have different effect on all-age group and AYA group. The underlying reason is unknown, and the possible reason is that different cancer may have different impact on life of quality and mental health of all-age patient and AYA patients (21,35,36). Also, AYA patients with different cancer may undergo different survivorship care patterns compared to cancer patients in other age (37).

When considering clinicopathological factors, localized tumor is related to higher risk of suicide in all-age cancer patients and AYA cancer patients. It has been reported that early stage is suicide risk factor of penile cancer patients (6). However, previous studies showed advanced stage cancer patients tend to suicide, which is different with our study (2,3,38). A possible reason is that patients with distant stage may die from the disease itself rather than suicide because of the poor prognosis of advanced cancer. Surgery is related to suicide in all-age cancer patients, but it doesn't have significant impact on suicide ideal in AYA cancer patients. Curative surgery may result in weakness and loss of autonomy in a population in older people, and AYA group patients may have stronger resistance to weakness caused by surgery (39).

Longer period from cancer diagnosis is associated with higher suicide risk of both all-age patient and AYA patients within 5 years from diagnosis. Previous study showed Austrian cancer patients is most likely to commit suicide within 1 year from diagnosis, which is different from our result (40). The different result may be explained by accumulated pain in treatment and poor quality of life in long-term survivors of cancer (41). When analyzed in specific cancer, breast cancer patients in all-age group have highest suicide risk in first year from cancer diagnosis, which is consistent with former research (7). In AYA group, cervical cancer patients have highest suicide risk in first year from cancer diagnosis. A possible reason is that cervical cancer may deprive fertility of AYA patients, leading to depression of AYA patients (42).

Besides demographic and clinicopathological factors mentioned above, suicidal behavior may also be influenced by personal and psychological factors (43,44). A prospective study reported that early onset of tobacco use increase risk of suicidal behaviors in AYA patients significantly (45). Use of alcohol and marijuana may also predict higher risk of suicide in AYA patients (46). Lower education level and unemployment caused by cancer may also associated with higher risk of suicide in AYA patients (44,47). In addition, infertility increased risk of suicidal attempts of AYA patients so it is important to preserve fertility of AYA patients during treatment of cancer (48).

Study limitations

Our study still has some limitations. SEER is a database only contains information of US cancer patients, so our study has a weakness of research area, and research over the world is still needed. Suicide is a complicated phenomenon affected by many factors, but detailed information such as socioeconomic status and treatment details is not available in SEER database.

Conclusions

Male sex, white race, unmarried status, localized cancer stage and longer survival time within first 5 year of cancer diagnosis are prevalent risk factors for both AYA group patients and all-age patients, and risk factors of suicide have similar effects on patients in different age groups. Therefore, it is unnecessary to separate AYA patients as a specific group to identify patients with higher suicide risk.

Acknowledgments

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Approval was waived by the local ethics committee, as SEER data is publicly available and de-identified. The study was exempted from Institutional Review Board approval, due to the use of a large cancer database with unidentifiable patient information.

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Table S1 Suicide mortality rate in all-age patients and AYA patients, SEER, 1973–2015

Cancer	All-age[a]	Suicide[b]	SMR (%)	AYA[c]	AYA suicide[d]	AYA SMR (%)	P[e]
Total	5,261,459	7,831	0.15	312,313	433	0.14	0.150
Nasopharynx	12,146	41	0.34	2,131	8	0.38	0.783
Esophagus	64,161	142	0.22	983	0	0.00	0.283
Stomach	136,555	196	0.14	6,186	8	0.13	0.772
Colon and rectum	609,617	945	0.16	21,235	43	0.20	0.085
Liver	107,008	60	0.06	2,920	1	0.03	0.621
Gallbladder	19,787	14	0.07	322	0	0.00	1.000
Pancreas	179,137	140	0.08	3,006	2	0.07	1.000
Lung	863,239	1,142	0.13	10,548	12	0.11	0.603
Bone	20,227	45	0.22	6,070	17	0.28	0.417
Melanoma	238,952	470	0.20	47,325	90	0.19	0.769
Breast	941,249	681	0.07	71,744	66	0.09	0.062
Cervix uteri	76,452	75	0.10	25,166	39	0.15	0.019
Uterus	206,425	114	0.06	9,715	8	0.08	0.271
Ovary	111,708	84	0.08	10,246	12	0.12	0.148
Prostate	972,409	2,553	0.26	1,038	3	0.29	1.000
Urinary bladder	235,969	604	0.26	5,130	19	0.37	0.110
Kidney & renal pelvis	176,646	242	0.14	10,192	13	0.13	0.802
Eye	15,750	33	0.21	1,523	3	0.20	1.000
Brain & other nervous system	115,698	109	0.09	21,417	44	0.21	<0.001
Thyroid	158,324	141	0.09	55,416	45	0.08	0.589

[a], number of all-age patients; [b], number of suicide all-age patients; [c], number of AYA patients; [d], number of suicide AYA patients; [e], P value of chi-square test. SEER, Surveillance, Epidemiology, and End Results; AYA, adolescence and young adult; SMR, suicide mortality rate.

Table S2 Trend of Suicide mortality SMR (%) in all-age cancer patients, SEER, 1973–2015

Cancer	Before 1993		1994–2003		After 2004		P[a]
	N	SMR (%)	N	SMR (%)	N	SMR (%)	
Total	2,807	0.27	2479	0.18	2,545	0.09	<0.001
Nasopharynx	11	0.43	17	0.51	13	0.21	0.036
Esophagus	34	0.25	40	0.23	68	0.20	0.512
Stomach	71	0.20	61	0.17	64	0.10	<0.001
Colon and rectum	380	0.25	273	0.17	292	0.10	<0.001
Liver	7	0.07	16	0.07	37	0.05	0.665
Gallbladder	5	0.10	4	0.08	5	0.05	0.593
Pancreas	31	0.09	34	0.08	75	0.08	0.836
Lung	410	0.21	354	0.15	378	0.09	<0.001
Bone	18	0.49	12	0.22	15	0.13	<0.001
Melanoma	138	0.41	165	0.29	167	0.11	<0.001
Breast	266	0.15	215	0.09	200	0.04	<0.001
Cervix uteri	36	0.18	23	0.11	16	0.05	<0.001
Uterus	59	0.13	23	0.05	32	0.03	<0.001
Ovary	36	0.13	24	0.08	24	0.04	<0.001
Prostate	887	0.55	910	0.34	756	0.14	<0.001
Urinary bladder	240	0.46	163	0.28	201	0.16	<0.001
Kidney and renal pelvis	76	0.30	64	0.16	102	0.09	<0.001
Eye	11	0.36	10	0.24	12	0.14	0.057
Brain and other nervous system	38	0.15	30	0.10	41	0.07	0.002
Thyroid	53	0.32	41	0.13	47	0.04	<0.001

[a], P value of chi-square test. SEER, Surveillance, Epidemiology, and End Results; SMR, suicide mortality rate.

Table S3 Trend of suicide mortality SMR (%) in AYA cancer patients, SEER, 1973–2015

Cancer	Before 1993		1994–2003		After 2004		P[a]
	N	SMR (%)	N	SMR (%)	N	SMR (%)	
AYA Total	197	0.30	138	0.17	98	0.06	<0.001
Nasopharynx	1	0.20	5	0.79	2	0.20	0.168
Esophagus	0	0.00	0	0.00	0	0.00	–
Stomach	1	0.08	3	0.17	4	0.13	0.808
Colon and rectum	14	0.37	15	0.28	14	0.12	0.004
Liver	0	0.00	0	0.00	1	0.07	1
Gallbladder	0	0.00	0	0.00	0	0.00	–
Pancreas	1	0.16	1	0.13	0	0.00	0.212
Lung	6	0.19	4	0.12	2	0.05	0.237
Bone	9	0.68	4	0.23	4	0.13	0.012
Melanoma	46	0.42	33	0.24	11	0.05	<0.001
Breast	27	0.17	23	0.12	16	0.04	<0.001
Cervix uteri	20	0.29	11	0.15	8	0.07	0.002
Uterus	3	0.17	2	0.08	3	0.05	0.294
Ovary	6	0.20	3	0.11	3	0.07	0.241
Prostate	1	1.59	0	0.00	2	0.30	0.198
Urinary bladder	9	0.56	6	0.41	4	0.19	0.196
Kidney and renal pelvis	7	0.52	4	0.18	2	0.03	<0.001
Eye	1	0.31	1	0.23	1	0.13	0.784
Brain and other nervous system	20	0.37	13	0.21	11	0.11	0.003
Thyroid	25	0.32	10	0.08	10	0.03	<0.001

[a], P value of chi-square test. SEER, Surveillance, Epidemiology, and End Results; AYA, adolescence and young adult; SMR, suicide mortality rate.