Acta Medica Academica 2012;41(2):154-160
DOI: 10.5644/ama2006-124.48

Suicide among childhood cancer survivors in Slovenia

Mojca Čižek Sajko[1], Niko Čižek[2], Berta Jereb[3]

[1] Institute for Biostatistics and Medical Informatics, Faculty of Medicine Ljubljana, Ljubljana, Slovenia
[2] Surveying Company Ljubljana Ljubljana, Slovenia
[3] Institute of Oncology, University Medical Centre Ljubljana Ljubljana, Slovenia

Corresponding author:
Mojca Čižek Sajko
Institute for Biostatistics and Medical Informatics
Faculty of Medicine
University of Ljubljana
Vrazov trg 2
1000 Ljubljana
Slovenia
mojca.cizek.sajko@gmail.com
Tel.: + 386 1 543 7770
Fax.: + 386 1 543 7771

Received: 3 October 2012
Accepted: 2 November 2012

Objective. Suicide is one of the causes of late mortality among childhood cancer survivors. The aim of our study was to analyse the risk of suicide among childhood cancer survivors compared with that of the general population of Slovenia. **Patients and methods**. This retrospective study included patients with childhood cancer registered at the Cancer Registry of Slovenia between 1978-2008, with an observation period of 1978-2010. Childhood cancer patients and control subjects from the general population of Slovenia were matched by sex, year and age at the beginning of follow-up and time of follow-up in years. Data on the general population of Slovenia were obtained from the Statistical Office of the Republic of Slovenia. **Results**. A total of 1647 patients were recorded in the Cancer Registry as having cancer during childhood, with 3 patients committing suicide. All three were male. Their age at diagnosis of cancer was 12, 13 and 2 years old; their age at suicide was 19, 32 and 28 years old. The mechanism of death was asphyxiation in all three deaths. The calculation of the expected number of suicides in the group of individuals with childhood cancer from the general Slovene population revealed the number of 3.16 persons. **Conclusion**. The comparison of the observed and expected probability showed that there was no statistically significant difference in the suicide rate between childhood cancer survivors and the general population of Slovenia.

Key words: Childhood cancer, Late mortality, Slovene population, Suicide risk.

Introduction

Suicide is the 13th leading cause of death in the world (1). In Slovenia, with a population close to 2 million, suicide accounts for 2.4% of all deaths in the general population (from the 10-14 years age group to the 80 years and above age group)(2). Slovenia is ranked fifth among European countries in terms of suicides (3).

One of the causes of late mortality in childhood cancer survivors is suicide.An increased risk of suicide has been reported among childhood cancer survivors (4, 5). It has been suggested that when viewed in the context of population–based studies of

suicide, adult survivors of childhood cancer have an elevated risk for suicidality (4, 5) while others have reported no correlation between childhood cancer associated with a risk of suicide (6, 7). The variation in the frequency of suicides among different countries (8) might be correlated to several cultural and behavioral factors, which also reflect suicidal behavior among childhood cancer survivors.

In an analysis of 228 childhood cancer survivors aged 18 to 61 years (114 women and 114 men), treated and followed up at the Oncological Institute in Slovenia, patients were matched by sex and age with a control group of individuals, who did not experience any chronical disease during childhood (9). However, the study showed there were higher rates of depression among childhood cancer survivors than among controls. Suicidal thoughts were, however, present in childhood cancer survivors in equal frequency as in the controls, and a plan for suicide was present in both groups in 8.7% (9). It has been recommended that depressive disorder should alert for risk assesment of suicidal adolescents (10).

The aim of this paper was to compare suicide frequency among children treated for cancer with the suicide frequency of the general population in Slovenia.

Materials and methods

Subjects

The study population was comprised of individuals with childhood cancer, registered with the Cancer Registry of Slovenia between 1978-2008 and treated at the Department of Oncology and Haematology of the University Children's Hospital in Ljubljana. The observation period was 1978–2010.

Inclusion criteria: diagnosis of childhood cancer, patient age at the start of observation ≥5 years old, first diagnosis made between 1978–2008, or year of first diagnosis before 1978, but patient still alive in 1978.

Exclusion criteria: nonresidents were excluded.

All children with cancer in Slovenia are treated at the Department of Oncology and Haematology of the University Children's Hospital in Ljubljana. After treatment, all are followed up by the same center for at least five years or until they reach the age of 18 years old. Since 1986, all childhood cancer survivors have been followed up regularly, at least once every year, at the outpatient Clinic for Late Effects at the Institute of Oncology, Ljubljana (11).

Demographic data (age, sex) and medical information on diagnosis, date of diagnosis and treatment were obtained from medical records, while information on patient status (alive/suicide/other cause of death) was obtained from the Cancer Registry of Slovenia or from the Clinic for Late Effects at the Institute of Oncology.

For the purpose of this study, subjects from the general population of Slovenia were used as a comparison group. Childhood cancer patients and control subjects from the general population were matched by the following characteristics: sex, year of the beginning of follow-up, age at the beginning of follow-up, and time of follow-up in years.

The year of the beginning of follow-up was either:

(a) the year of diagnosis between 1978–2008 if at diagnosis the patient was aged 5 years or more, or

(b) the year of patient's age of 5 years if the diagnosis was set between 1978–2008 and at diagnosis the patient was younger than 5 years, or

(c) the year of patient's age of 5 years if the diagnosis was set before 1978 and in 1978 the patient was younger than 5 years, or

(d) the year when observation period started (i.e. the year 1978) if the diagnosis was set before 1978 and in 1978 the patient was still alive and aged 5 years or more.

The time of follow-up was defined as the time from diagnosis or first year of the beginning of follow-up to the event, which was defined as suicide, death to other causes, or year of last follow-up (i.e. 2010 was taken as the end of the observation period, or some earlier year if the patient was lost from follow-up).

Data on the general population of Slovenia were obtained from the Statistical Office of the Republic of Slovenia, SORS (12). As the data on death to suicides in Slovenia were recorded at SORS separately by sex as late as 1978, we had to adjust our observation period to 1978 – 2010, although the first records in the Cancer Registry of Slovenia dated from 1950.

Statistical analysis

Basic demographic and clinical characteristics were presented using descriptive statistics. The SORS reports data on the general population and deaths in 5-years age groups, our data is reported in a similiar manner. Descriptive analysis was carried out using SPSS 20.0 statistical software (SPSS Inc., Chicago; IL, USA), while the R language (13) was used for inferential analysis.

To compare the observed number of suicides from the patient population and the expected number of suicides, if we assume that the suicide rate among cancer patients is smiliar to that of the general population, the binomial test was applied. The expected number of suicides in the patient population was calculated from the general Slovene population, comparable to the patient population in terms of 4 characteristics, noted in the Subjects section. To locate the comparable general population group and for calculating the expected number of suicides, a special programme in R language was used, prepared at the Institute for Biostatistics and Medical Informatics in Ljubljana specifically for this purpose.

The expected number of suicides was calculated as follows: in the general population, for each patient a comparable individual, in terms of sex, year and age at the beginning of follow-up, was looked for. For this individual, on the basis of data of the number of suicides and the number of residents the probability of suicide was calculated for each year of follow-up. Finally, the probabilities of suicides for all years of follow-up were summed up, which gave us the expected number of suicides in the study population according to the general population for this specific patient. To gain the overall expected number of suicides, all probabilities summed up per patient were summed up for all patients.

Results

A total of 1647 individuals with cancer during childhood were included in the analysis. Demographic and clinical information is presented in Table 1. Patients were followed up from 1 to 33 years. At the end of the follow-up period, the individuals' ages ranged from 5 to 66 years old, with the majority (43%) of them 20 to 39 years old. The most frequent diagnosis was leukemia (26%) and tumors of the central nervous system (19%). The majority of patients were treated with both irradiation and chemotherapy (29%),

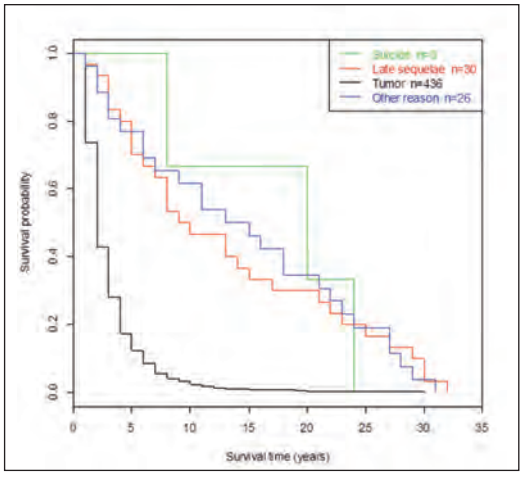

Figure 1 Estimated survivorship functions for subjects in respect to cause of death.

Table 1 Demographic and clinical characteristics of individuals with childhood cancer

Characteristic	Subjects (n=1647)
Age at cancer diagnosis, years	8.2 (4.9), [0-18]
Age at the beginning of the follow-up, years	9.4 (4.4), [5-34]
Age at the end of the follow-up, years	22.3 (11.9), [5-66]
Age at the end of the follow-up, n (%)	
<10 years	261 (16)
10-19 years	507 (31)
20-39 years	708 (43)
≥40 years	171 (10)
Time of observation, years	13.9 (10.7), [1-33]
Sex, n (%)	
Female	713 (43)
Male	934 (57)
Cancer diagnosis, n (%)	
Leukemia	430 (26)
Central nervous system	317 (19)
Hodgkin's disease	150 (9)
Non-Hodgkin's lymphoma	140 (9)
Renal tumors	94 (6)
Neuroblastoma	59 (4)
Rhabdomyosarcoma	62 (4)
Malignant bone tumors / Ewing's and PNET	111 (7)
Soft-tissue sarcomas	54 (3)
Gonads	55 (3)
Carcinomas	109 (7)
Other neoplasms	51 (3)
Unspecified malignant neoplasms	15 (1)
Cancer treatment*, n (%)	
SR=Surgery	232 (14)
RT=Radiation therapy	41 (2)
ChT=Chemotherapy	235 (14)
SR + RT	169 (10)
RT + ChT	478 (29)
SR + ChT	230 (14)
SR + RT + ChT	243 (15)

Values are mean (standard deviation) and [min, max], unless otherwise specified. *Missing data in six patients; percentages calculated per 1641 subjects. PNET=Primitive neuroectodermal tumor.

while 8 (0.5%) patients received no therapy because they had died before therapy started, and 5 (0.3%) had no treatment (four with IV S neuroblastoma and one with brain tumor).

At the end of the follow-up, 1152 (70%) individuals were still alive, while 495 (30%) had died. According to the cause of death, estimated survivorship functions are shown in Figure 1. The longest median survival time was recorded for deaths from suicide (20 years), a shorter median survival time was recorded for deaths due to other reasons

Table 2 Comparison of observed and expected probability of suicide, calculated by binomial test

	Observed	Expected	P value
Number of suicides	3	3.1555	-
Probability of suicides	3/1647=0.0018214	3.1555/1647=0.0019159	1

Table 3 Demographic and clinical characteristics of individuals who committed suicide

Characteristic	Person 1	Person 2	Person 3
Sex	Male	Male	Male
Diagnosis	Osteogenic sarcoma	Brain tumor	Soft tissue sarcoma
Treatment	SR+ChT	SR+RT	SR+ChT
Year of birth	1966	1974	1981
Age at diagnosis (yrs)	12	13	2
Date of suicide	May 1985	July 2006	June 2009
Time of follow-up (yrs)	7	19	23
Age at suicide (yrs)	19	32	28
Method of suicide	Strangulation	Strangulation	Strangulation

ChT=chemotherapy; RT=radiation therapy; SR=surgery.

(injury, traffic accident, asphyxiation) and due to late sequelae (13 and 9 years, respectively), while the shortest median survival time was observed for deaths because of the primary malignant disease (2 years).

Out of 1647 individuals, only 3 suicides were recorded during the observation period. The calculation of the expected number of suicides in the group of individuals with childhood cancer from the general Slovene population was 3.1555 persons. The probability of suicide, calculated from among the study population, was 0.0018214, (95% confidence interval: 0.0003758-0.0053139). The comparison of observed and expected probability showed that there was no statistically significant difference between the two groups (p=1) (Table 2). The characteristics of the three individuals that committed suicide are shown in Table 3.

Discussion

Suicide is a significant public health issue in Slovenia and around the world. Any attempt to ascertain the reason for committing suicide may prevent future acts. In this current study, we identified 3 suicides among patients treated for childhood cancer. All the victims were males aged 19, 32 and 28 years old. This study provided some insight into the possible reasons that triggered suicide. One patient (Patient #1) was dissatisfied due to physical distress following exarticulation of the femur, while another patient (Patient #2) was distressed following treatment by cranial radiation. These two patients did not have regular follow-up. Some reports have cited that dissatisfaction with physical appearance, poor physical health and treatment with cranial radiation were associated with psychological distress (14). Cranial radiotherapy, causing a specific pattern of cognitive and educational sequelae, is associated with suicidal ideation (15). The third patient, who was regularly followed at the outpatient clinic for late effects, was in perfect health with no complaints 19 months prior to death. The reason for the suicide was not determined, although it was reported that he consumed huge amounts of alcohol.

None of these three patients were included in the group of childhood cancer survivors analysed for depression conducted in 2006 (9). In that study 146 childhood cancer survivors, all under 18 years old at diagnosis, were followed up at the Oncological Institute in Ljubljana (9). About 40% of them reported that they thought they would rather be dead, among them twice as many women, 29% had active suicide thoughts, while 8.7% had a suicide plan. Seven (7/146, 5%) survivors actually tried to commit suicide, in comparison with one (1/87, 1%) in the control group. This was the only statistically significant ($p<0.001$) difference comparing the depressive symptoms of the study group and the control group. There were no successful suicides among the childhood cancer survivors. It would seem that subjects with the experience of childhood cancer appreciate life in a way which protects them from committing suicide.

Also among those survivors who had been attending group meetings (once per month), only a half of them reported depressive symptoms (9).

In a study by Recklitis (14), childhood cancer survivors who completed screening with the Symptom Checklist 90 Revised (SCL-90), reported little (15%) or no (84%) distress, but had a positive screen on the Mental Scale, indicating significant psychological distress. Suicidal symptoms were reported in 14% of the children. Though it noted important differences, risk factors for suicide attempts and completion are well established (16), it still seems hard to predict suicide in a certain individual.

Regarding reports of the high risk for suicide among childhood cancer survivors a question arose: Have any of those survivors in the study, whose responses led the investigators to conclude that they were at risk for suicide actually committed suicide after the completion of data collection? Zebrack proposed an analysis that would have made a comparison to see if the same respondents who indicated suicidality in their survey also were assesed and indentified by clinicians as demonstrating indicators of suicide risk ideation (17).

In our study, the observed suicide frequency among children treated for cancer did not differ from the expected frequency in to the general Slovene population (3 versus 3.16, $p=1$). Slovenia is a small country, with only 2 million inhabitants, so it is hard to make conclusions in this respect. However, our results were similar to previously published large-scale studies which suggest the risk of suicides in survivors does not exceed the risk observed in the appropriately matched general populations (18-23). However, a recent review reports evidence that the prevalence of completed suicides is greater in a cancer population than in the general population (16).

In countries where suicide research is strong, suicide rates have been declining due to universal preventive interventions. As pointed out by Nordentoft (24), suicide is a major public health problem and it should be given high priority with regard to prevention and research.

Authors' contributions: Conception and design: BJ; Acquisition, analysis and interpretation of data: BJ, NČ, MČS; Drafting the article: BJ, MČS; Revising it critically for important intellectual content: BJ, NČ, MČS.

Conflict of interest: The authors declare that they have no conflict of interest. This study was not sponsored by any external organization.

References

1. Krug EG. World Report on Violence and Health. World Health Organization. Geneva; 2002.
2. Statistical Yearbook 2010 (database on the Internet]. SORS [cited 2012 Aug 20]. Available from: http://www.stat.si/letopis/LetopisVsebina.aspx?poglavje=4&lang=si&leto=2010
3. Death due to suicide [database on the Internet]. EUROSTAT [updated 2012 Apr 02; cited 2012

Aug 20]. Available from: http://epp.eurostat.ec.europa.eu/tgm/table.do?tab=table&init=1&plugin=0&language=en&pcode=tps00122

4. Recklitis CJ, Diller LR, Li X, Najita J, Robinson LL, Zeltzer L. Suicide ideation in adult survivors of childhood cancer: a report from the Childhood Cancer Survivor Study. J Clin Oncol. 2010;28(4):655-61.
5. Howard RA, Inskip PD, Travis LB. Suicide after childhood cancer. J Clin Oncol. 2007;25(6):731.
6. Mertens AC. Cause of mortality in 5-year survivors of childhood cancer. Pediatr Blood Cancer. 2007;48(7):723-6.
7. Teta MJ, Del Po MC, Kasl SV, Meigs JW, Myers MH, Mulvihill JJ. Psychosocial consequences of childhood and adolescent cancer survival. J Chronic Dis. 1986;39(9):751-9.
8. Centers of Disease Control and Prevention (CDC). Rates of homicide, suicide, and firearm–related death among children – 26 industrialized countries. MMWR Morb Mortal Wkly Rep. 1997;46(5):101-5.
9. Svetičič J, Marušič A, Jereb B. Ali je med preživelimi raka v otroštvu več depresivnosti in samomorilnega vedenja? Onkologija. 2006;10(2):75-80.
10. Nrugham I, LarssonB, Sund AM. Specific depressive symptoms and disorders as associates and predictors of suicidal acts across adolescence. J Affect Disord. 2008;111(1):83-93.
11. Jereb B. Model for long-term follow–up of survivors of childhood cancer. Med Pediatr Oncol. 2000;34(4):256-8.
12. Statistical Office of the Republic of Slovenia [homepage on the Internet]. Ljubljana: The Statistical Office [cited Aug 22]. Available from: http://www.stat.si/eng/index.asp
13. R Core Team [homepage on the Internet]. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna (Austria); ISBN: 3-900051-07-0; c2012 [cited Aug 22]. Available at: http://www.R-project.org
14. Recklitis CJ, Lockwood RA, Rothwell MA, Diller LR. Suicidal ideation and attempts in adult survivors of childhood cancer. J Clin Oncol. 2006;24(24):3852-7.
15. Recklitis C, O'Leary T, Diller L. Utility of routine psychological screening in the childhood cancer survivor clinic. J Clin Oncol. 2003;21(5):787-92.
16. Robson A, Scrutton F, Wilkinson L, MacLeod F. The risk of suicide in cancer patients: a review of the literature. Psychooncology. 2010;19(12):1250-8.
17. Zebrack BJ, Ell K, Smith WB. Suicide Risk in Childhood Cancer Survivors. J Clin Oncol. 2007;25(6):732-3.
18. Mertens AC, Yasui Y, Neglia JP, Potter JD, Nesbit ME Jr, Ruccione K, et al. Late mortality experience in five-year survivors of childhood and adolescent cancer: the Childhood Cancer Survivor Study. J Clin Oncol. 2001;19(13):3163-72.
19. Möller TR, Garwicz S, Barlow L, Falck Winther J, Glattre E, Olafsdottir G, et al. Decreasing late mortality among five-year survivors of cancer in childhood and adolescence: A population-based study in the Nordic countries. J Clin Oncol. 2001;19(13):3173-81.
20. Robertson CM, Hawkins MM, Kingston JE. Late deaths and survival after childhood cancer: implications for cure. BMJ. 1994;309(6948):162-6.
21. Hawkins MM, Kingston JE, Kinnier Wilson LM. Late deaths after treatment for childhood cancer. Arch Dis Child. 1990;65(12):1356-63.
22. Hudson MM, Jones D, Boyett J, Sharp GB, Pui CH. Late mortality of long-term survivors of childhood cancer. J Clin Oncol. 1997;15(6):2205-13.
23. Cardous-Ubbink MC, Heinen RC, Langeveld NE, Bakker PJ, Voûte PA, Caron HN, et al. Long-term cause-specific mortality among five-year survivors of childhood cancer. Pediatr Blood Cancer. 2004;42(7):563-73.
24. Nordentoft M. Prevention of suicide and attempted suicide in Denmark. Epidemiological studies of suicide and intervention studies in selected risk groups. Dan Med Bull. 2007;54(4):306-69.