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Death by suicide and other externally caused injuries following a cancer diagnosis: the Japan Public Health Center-based Prospective Study

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Abstract

***Objective*: There have been very few population-based prospective studies that have investigated the risks of deaths by suicide and other externally caused injuries (ECIs) among cancer patients in an Asian population. This study investigated whether the risk of death by both suicide and ECIs increases during the first year following the initial diagnosis of cancer.**

***Methods*: Data were analyzed from a population-based cohort of Japanese residents between 1990 and 2010, collected during the Japan Public Health Center-based Prospective Study. Poisson regression models were used to calculate adjusted risk ratios (RRs) for both suicide and ECI deaths. To adjust for unmeasured confounding factors, case-crossover analyses were conducted for all patients with cancer who died by suicide and ECIs.**

***Results*: A population-based cohort of 102,843 Japanese residents was established. During the follow-up period, there were 34 suicides and 48 ECI deaths among patients with cancer, as compared with 527 suicides and 707 ECI deaths among those who did not have cancer. Analyses revealed that those who were newly diagnosed with cancer were at a greatly increased risk of death by suicide and ECIs within the first year after their diagnosis (suicide RR = 23.9, 95% CI: 13.8–41.6; ECI RR = 18.8, 95% CI: 11.4–31.0). Furthermore, the case-crossover analyses generally confirmed the results of the Poisson regressions.**

***Conclusions*: The risks of suicide and ECI deaths within the first year after a cancer diagnosis were higher than those among cancer-free populations. A diagnosis of cancer is a critical experience that may increase the risk of fatal outcomes.**

Introduction

Patients with cancer are at an increased risk of suicide [1–6], with elevated risk levels during the first year following the initial diagnosis [7–14]. Impairment of physical and/or social functioning, such as cognitive dysfunction caused by chemotherapy [15], or psychological stress induced by a cancer diagnosis [16,17] and postcancer impairment would increase the risk of death by suicide.

It has also been argued that a diagnosis of cancer is associated with increased risk of death by other externally caused injuries (ECIs), including death due to accidents or events of undetermined intent [18–20]. For instance, impairment of physical and social functioning caused by treatment [15] would increase the risk of death by ECI.

It is anticipated that physical and/or social impairment may be common background factors shared between suicide and ECI deaths after a cancer diagnosis. Furthermore, previous studies suggest that some deaths classified as ECI deaths might be suicides, and the risk factors for suicide and accidental death might be similar [21–26]. Thus, it is necessary to examine not only the risk of suicide but also the risk of ECI deaths following a cancer diagnosis.

There have been very few population-based prospective studies to investigate the period of highest risk of both suicide and ECI deaths after a cancer diagnosis in an

Asian population. Thus, the current study examined whether the risk of death by both suicide and ECIs increases during the first year following the initial diagnosis of cancer, using data from the Japan Public Health Center-based Prospective Study (JPHC Study), a large prospective cohort study.

Methods

Study design

The JPHC Study began in 1990 for Cohort I and in 1993 for Cohort II. The study population included Japanese residents aged 40–59 years in Cohort I and those aged 40–69 years in Cohort II at baseline. Participants were recruited from 10 public health center areas. These areas were selected in consideration for the variation of mortality rate, geographical distribution, and feasibility. The JPHC Study design has been reported in detail previously [27].

This study protocol was approved by the Institutional Review Board of the National Cancer Center, Tokyo, Japan. Informed consent was obtained from study participants implicitly when they completed the baseline survey in which the purpose and follow-up methods of the JPHC Study were described.

Baseline survey

A self-administered questionnaire was distributed to all registered residents at baseline to obtain information regarding sociodemographic characteristics, such as cohabitation status, and medical history of cancer. We used self-reported cancer to exclude participants with a history of cancer at baseline from data analyses.

Follow-up

The residential registry in each area was reviewed annually to obtain information on changes in residence status. In Japan, the Basic Resident Registration Act requires registration of residency, and the registry is considered complete [28]. Data on participant deaths were based on death certificates obtained from the public health centers. All study subjects were followed until their date of death or emigration from the study area, or 31 December 2010 (the study period end date). Persons who were lost to follow-up were censored at the last confirmed date of presence in the study area.

Ascertainment of cancer

Cancers were identified through active patient notification from local major hospitals in the study area and by data linkage with population-based cancer registries [28]. To obtain information on cancer incidence more completely, death certificates were used as a supplementary information source. The patients were coded according to the *International Classification of Diseases for Oncology, Third Edition* (ICD-O-3).

Incidence of suicide and ECI deaths

Death by suicide was defined according to the ICD-10, as codes X60-X84. Similarly, ECI deaths included both accidental deaths (ICD-10 codes V01-X59) and deaths due to events of undetermined intent (ICD-10 codes Y10-Y34).

Statistical analysis

The analysis strategy in the present study followed that of Fang *et al.* [13] Initially, unadjusted incidence rates were calculated for suicide and ECI deaths among people with cancer diagnoses and those without cancer diagnoses. In calculating risk ratios (RRs), suicide rates among the cancer group were compared with those among the cancer-free group, and incidence rates of ECIs among the cancer group were compared with those among the cancer-free group. We used Poisson regression models with the number of deaths by suicide and ECIs as the dependent variable and the log person-years as an offset variable to calculate adjusted RRs and 95% confidence intervals (CI). In Poisson regression models, RRs were adjusted for sex, age at study entry, cohabitation status (cohabitation or no cohabitation), employment status (employed or unemployed, which includes those not in the labor force such as homemakers), and cohort (Cohort I or Cohort II). Time after cancer diagnosis was defined as within 1 year, or beyond 1 year.

Furthermore, to adjust for unmeasured confounding factors, a case-crossover analysis [13,29,30] was performed for all patients with cancer who died by suicide or ECIs. In a recent epidemiological study [13], a case-crossover analysis was performed supplementarily to confirm the findings obtained from the other method of analysis (i.e., Poisson regression models in the current study). The occurrence of a cancer diagnosis in the prespecified hazard period, which was defined as the 52 weeks (i.e., 1 year) preceding deaths from suicide and ECIs, was compared with that in the control period, which was defined as the 352 weeks preceding the hazard period, on the basis of a previous epidemiological study concerning the risk of suicide after a cancer diagnosis [13]. In our case-crossover analysis, cancer patients who died by suicide and ECIs served as their own controls, and different periods for the same patients were compared. For both deaths, the Mantel–Haenszel method was used to estimate RRs by comparing the risk in the hazard period with that of the control period.

Analyses were conducted using SAS version 9.3 (SAS Institute, Cary, NC, USA).

Results

Of 133,076 people who were eligible for the current study, 106,325 participants (50,439 men and 55,886 women) responded to the questionnaire at baseline (response rate, 79.9%). Of the respondents, 911 were excluded because of missing or incorrect data about their demographical variables, 2139 were excluded because of having a past history of cancer, and 432 were excluded because of missing or incorrect data on cancer status. Thus, a population-based cohort of 102,843 Japanese residents (49,033 men and 53,810 women) was established (Figure 1). Table 1 summarizes the baseline characteristics of the participants.

Of the 102,843 participants, 14,540 (14.1%) died from various causes, 10,271 (10.0%) emigrated from the study area, and 60 (0.1%) were lost to follow-up. During the follow-up period, 11,187 patients were identified as having received a first-time cancer diagnosis.

Suicide after cancer diagnosis

During the follow-up period, there were 34 cases of suicide among cancer patients, and 527 cases of suicide among those who were cancer-free. An increased level of risk was particularly prominent among cancer patients during their first year after diagnosis, as compared with cancer-free people (Table 2). The adjusted RR of suicide within 1 year after a cancer diagnosis was 23.9 (95% CI: 13.8–41.6). However, the RR decreased dramatically beyond the first year after the diagnosis (RR = 1.1, 95% CI: 0.7–1.8).

In terms of the level of clinical deterioration at the time of diagnosis, adjusted RRs were 1.5 (95% CI: 1.0–2.5) among patients with localized cancer and 2.3 (95% CI: 1.3–3.9) among patients with regional or distant cancer. As compared with those who were cancer-free, RRs of suicide among patients receiving a cancer diagnosis were 1.7 (95% CI: 1.2–2.6) among men and 2.1 (95% CI: 1.1–4.2) among women.

In the case-crossover analysis, 13 cases of suicide were observed within the hazard period and 18 cases within the control period (Table 3). Regardless of the period, hanging was the most frequent method of suicide among patients with cancer. The RR of suicide was 13.0 times (95% CI: 2.0–86.2) higher during the first year after a cancer diagnosis than during the control period (Table 4).

Externally caused injury deaths after cancer diagnosis

By the end of 2010, there were 48 ECI deaths among cancer patients and 707 ECI deaths among the cancer-free population. Consistent with results regarding the risk of suicide after a cancer diagnosis, the risk of ECI deaths was remarkably higher during the first year after the initial cancer diagnosis (Table 5). As compared with the

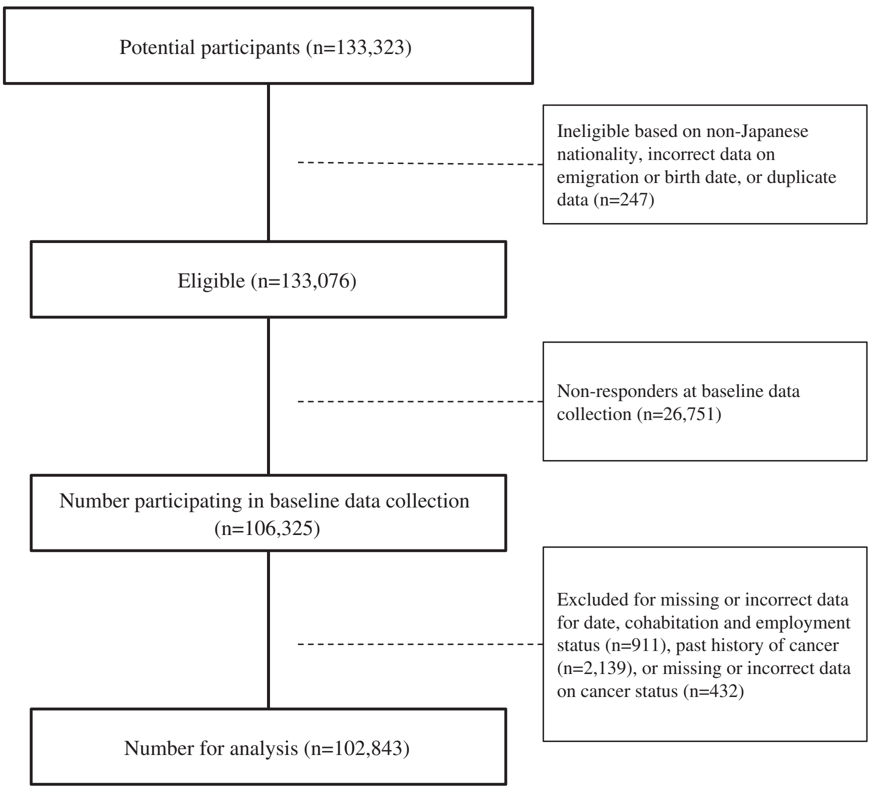

Figure 1. Flow diagram of participant selection

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Table 1. Baseline characteristics of the study participants for analysis

	Men	Women
Number of participants	49,033	53,810
Age group (years; %)		
40–64	92.2	91.4
65 and older	7.8	8.6
Mean (SD) (year)	51.6 (8.0)	51.9 (8.0)
Cohabitation status (%)		
Cohabitation	96.7	95.1
No cohabitation	3.3	4.9
Employment status (%)		
Employed	93.1	58.6
Unemployed	6.9	41.4

SD, standard deviation.

cancer-free population, the adjusted RR of ECI deaths within 1 year after the diagnosis was 18.8 (95% CI: 11.4–31.0). The RR decreased sharply beyond the first year after the diagnosis (RR = 1.2, 95% CI: 0.8–1.7).

In terms of the level of clinical deterioration at the time of diagnosis, adjusted RRs were 1.8 (95% CI: 1.2–2.6) among patients with localized cancer and 1.8 (95% CI: 1.1–3.0) among those with regional or distant cancer. As compared with those who were cancer-free, RRs of ECI deaths among patients receiving a cancer diagnosis were 1.5 (95% CI: 1.0–2.1) among men and 2.8 (95% CI: 1.6–4.7) among women.

In the case-crossover analysis, there were 16 cases of ECI deaths during the hazard period and 22 ECI deaths in the control period (Table 4). The RR of ECI deaths was 12.1 times (95% CI: 3.7–39.6) higher in the first year after a cancer diagnosis as in the control period.

Discussion

This study examined not only the risk of suicide but also the risk of ECI deaths among patients with cancer, using a population-based prospective cohort in Japan. For both suicide and ECI deaths, adjusted RRs within the first year following a cancer diagnosis were approximately 20-fold higher than the cancer-free population, and the risks decreased sharply after 1 year.

Recent studies have suggested that the first year, and particularly the first month, after a cancer diagnosis appears to be highly stressful for patients [12–14]. In the

Table 2. Incidence rates and risk ratios (RRs) of suicide after a cancer diagnosis

	Number of cases	Person-years	Incidence rates per 100,000 person-years	Unadjusted RR	Adjusted RR[a]	(95% CI)		
Time after diagnosis (years)								
0–1	13	1,264.1	1,028.4	30.6	23.9	13.8	—	41.6
1+	21	48,620.5	43.2	1.3	1.1	0.7	—	1.8
Cancer-free	527	1,569,244.3	33.6	1.0				
Stage								
Localized	17	28,776.9	59.1	1.8	1.5	1.0	—	2.5
Regional or distant	13	15,345.5	84.7	2.5	2.3	1.3	—	3.9
Cancer-free	527	1,569,244.3	33.6	1.0				
Sex								
Male								
Cancer	25	27,450.7	91.1	1.7	1.7	1.2	—	2.6
Cancer-free	371	703,217.1	52.8	1.0				
Female								
Cancer	9	22,433.9	40.1	2.2	2.1	1.1	—	4.2
Cancer-free	156	866,027.2	18.0	1.0				
Age (years)								
40–64								
Cancer	31	43,449.7	71.3	2.1	1.9	1.3	—	2.8
Cancer-free	488	1,466,802.8	33.3	1.0				
65 and older								
Cancer	3	6,434.9	46.6	1.2	1.2	0.4	—	3.8
Cancer-free	39	102,441.6	38.1	1.0				
Cohort								
Cohort I								
Cancer	20	43,449.1	86.6	2.3	2.2	1.4	—	3.5
Cancer-free	261	707,894.0	36.9	1.0				
Cohort II								
Cancer	14	26,788.5	52.3	1.7	1.4	0.8	—	2.5
Cancer-free	266	861,350.3	30.9	1.0				

[a]Risk ratios were adjusted for age at entry, sex, cohabitation status, employment status, and cohort.

Table 3. Number of deaths by cause of death and period in case-crossover analysis

Cause of death	ICD-10 code	Number of deaths among people with cancer diagnosis[a] Control period	Hazard period
Suicide	Self-poisoning by drugs, gasses, or pesticides (X60-X69)	2	2
	Hanging (X70)	13	9
	Jumping from a high place (X80)	2	1
	Other means (X71-79, X81-X84)	1	1
Externally caused injuries	Transportation accidents (V01-V99)	6	1
	Accidental falls (W00-W19)	3	3
	Accidental threats to breathing such as drowning (W65-W84)	12	7
	Other accidental injury (W20-W64, W85-X59)	1	4
	Event of undetermined intent (Y10-Y34)	0	1

ICD-10, International Statistical Classification of Diseases and Related Health Problems 10th Revision.
[a]For both suicide and externally caused injuries, the hazard period was defined as the 52 weeks preceding death and the control period as the 352 weeks preceding the hazard period.

Table 4. Case-crossover analysis of suicide and externally caused injuries (ECIs) after a cancer diagnosis

Cause of death	Number of deaths among people with cancer diagnosis[a] Control period	Hazard period	Risk ratio	(95% CI)		
Suicide	18	13	13.0	2.0	—	86.2
ECI	22	16	12.1	3.7	—	39.6

[a]For both suicide and externally caused injuries, the hazard period was defined as the 52 weeks preceding death and the control period as the 352 weeks preceding the hazard period.

Table 5. Incidence rates and risk ratios (RRs) of externally caused injury deaths after a cancer diagnosis

	Number of cases	Person-years	Incidence rate per 100,000 person-years	Unadjusted RR	Adjusted RR[a]	(95% CI)		
Time after diagnosis (years)								
0–1	16	1,264.1	1,265.7	28.1	18.8	11.4	—	31.0
1+	32	48,620.5	65.8	1.5	1.2	0.8	—	1.7
Cancer-free	707	1,569,244.3	45.1	1.0				
Stage								
Localized	29	28,776.9	100.8	2.2	1.8	1.2	—	2.6
Regional or distant	15	15,345.5	97.7	2.2	1.8	1.1	—	3.0
Cancer-free	707	1,569,244.3	45.1	1.0				
Sex								
Male								
Cancer	33	27,450.7	120.2	1.6	1.5	1.0	—	2.1
Cancer-free	514	703,217.1	73.1	1.0				
Female								
Cancer	15	22,433.9	66.9	3.0	2.8	1.6	—	4.7
Cancer-free	193	866,027.2	22.3	1.0				
Age (years)								
40–64								
Cancer	40	43,449.7	92.1	2.3	2.0	1.5	—	2.8
Cancer-free	592	1,466,802.8	40.4	1.0				
65 and older								
Cancer	8	6,434.9	124.3	1.1	0.9	0.4	—	1.8
Cancer-free	115	102,441.6	112.3	1.0				
Cohort								
Cohort I								
Cancer	22	23,096.1	95.3	2.5	2.3	1.5	—	3.5
Cancer-free	275	707,894.0	38.8	1.0				
Cohort II								
Cancer	26	26,788.5	97.1	1.9	1.4	0.9	—	2.1
Cancer-free	432	861,350.3	50.2	1.0				

[a]Risk ratios were adjusted for age at entry, sex, cohabitation status, employment status, and cohort.

present study, Poisson regression models revealed that those who were newly diagnosed as having cancer were at a remarkably increased risk of suicide within the first year after the diagnosis. These findings are consistent with previous studies suggesting that the emotional stress evoked by a cancer diagnosis [13] and impairment of physical and social functioning caused by treatment [15] elevate the immediate risk of suicide.

The risk of suicide within the first year after a cancer diagnosis was found to be approximately 20 times higher than that in the cancer-free population, a value higher than those documented in previous studies in Western countries [7–10]. The number of suicides observed in our population-based prospective cohort was small, and these small numbers could have contributed to the relatively high RRs. Furthermore, as suggested by previous literature [11], differences among population-based studies from several countries may be due to differences in the suicide rates of the general populations of the respective countries. This may be in addition to other factors, such as study design, improvements in cancer survival rates, sociocultural backgrounds (e.g., the psychological and/or economic burden of cancer may be heavier in Japan than in Western countries), and cancer care systems (e.g., psychosocial support after a cancer diagnosis might be less developed in Japan than in Western countries, especially during early follow-up periods). These background factors may have influenced the risk of suicide among cancer patients within the first year following a cancer diagnosis.

Studies have suggested that the risk of suicide after a cancer diagnosis is higher among patients with a poor prognosis [9,11], such as remote metastasis, at the time of the initial diagnosis. However, the present study did not observe a significantly elevated risk of suicide according to the clinical stage of cancer. This would be because the present study combined 'regional' and 'distant' metastasis categories into a single 'regional or distant' category, because of the small number of suicide cases in our population-based prospective cohort. It may also be possible that in Japan, where the percentage of physicians who disclose a cancer diagnosis to patients is lower than that in other developed countries [31], the impact of receiving a cancer diagnosis itself increases the risk of suicide, regardless of clinical stage or possibility of treatment.

Among people aged 40–64 years, the RR of suicide in cancer patients compared with the risk in the cancer-free population was 1.9. A plausible explanation for this increased risk is that, as implied by researchers [11], younger patients are more likely to face difficulties in making the psychological adjustments that are triggered by the thwarting of their life goals and the failure to fulfill their social roles, than are older people.

As shown in Table 3, hanging was the most frequent method of suicide among patients with cancer. This is consistent with the situation observed in the general Japanese population.

As researchers suggested [13], unmeasured confounding factors, such as depression at the baseline, among cancer and suicide may contribute to our findings in the Poisson regression models. However, the case-crossover analysis [13,29,30] with adjustment of unmeasured confounders, which compared different periods for the same patients, generally showed the same results as the main analyses, thereby allaying any concerns.

This study examined not only the high risk period for suicide but also high risk period for ECI deaths after a cancer diagnosis in an Asian population, using a large prospective cohort. Interestingly, consistent with the findings concerning the risk of suicide after a cancer diagnosis, a diagnosis of cancer remarkably increased the risk of ECI deaths within the first year following a diagnosis, with the risk decreasing sharply over the course of the initial year. Cancer incidence is associated with mental distress [16,17], cognitive dysfunction due to treatments [15], other physical illnesses such as cardiovascular events [13], and deterioration of social and physical function, all of which may increase the risk of ECI deaths among patients with cancer. The combination of mental distress and reduced impulse control or executive function due to treatment of cancer could increase the risk of ECI deaths.

Another possible reason for the similarities in increased risk after a cancer diagnosis between suicide and ECI deaths is that, as suggested by previous literature [21–26], some deaths classified as accidental deaths or deaths of undetermined intent may be probable suicides. As argued by researchers [32–34], the quality of cause-of-death coding and the completeness of suicide case ascertainment may be causes for concern. In Japan, death registration is mandatory, and death certificates must be completed by physicians. Additionally, all determinations of suicide are based on the results of medicolegal examinations by licensed physicians, as well as police investigation. The recording system for these data remained unchanged throughout the study period. Thus, suicide and ECI data used in the present study are believed to be sufficient in terms of quality and completeness.

The strengths of the current study include its population-based prospective design, which makes it possible to avoid selection or recall biases; its large sample and high response rate (approximately 80%); and its low rate of loss to follow-up.

On the other hand, the present study has some limitations worth noting. First, the number of suicides and ECI deaths among patients with cancer included in this population-based prospective cohort was not sufficient to allow for calculation of mortality rates by cancer site. Second, subjects in the current study were restricted to Japanese residents aged 40 years or older. In addition, residents of

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Tokyo (i.e., the largest city in Japan) were not included in the current analysis because of incomplete registration of cancer diagnoses at the public health center in Tokyo. Therefore, the applicability of our findings to populations with different backgrounds (e.g., younger populations, metropolitan populations within Japan, and populations living in other countries with lower suicide rates than Japan) should be considered.

In conclusion, in Japan, adjusted RRs of both suicide and ECI deaths within the first year following a cancer diagnosis were increased approximately 20-fold, in comparison with the cancer-free population. A cancer diagnosis is a critical experience that may lead to the deterioration of social and physical functions and may induce increases in the risk of fatal outcomes. Clinicians and healthcare professionals should be aware of the increased risk for various causes of death following a cancer diagnosis and should assess patients for emotional distress (e.g., by identifying and assessing symptoms of depression, suicidal thoughts, and physical or social impairments) at the time of the initial diagnosis and during the year following a cancer diagnosis.

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Conflict of interest

The authors have no conflicts of interest to disclose.

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