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審査学位論文
(博士)

Population-Based Incidence of Sudden Cardiac and Unexpected Death Before and After the 2011 Earthquake and Tsunami in Iwate, Northeast Japan

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Background—The aim of this study was to evaluate the temporal impact of the 2011 Japan earthquake and tsunami on the incidence of sudden cardiac and unexpected death (SCUD).

Methods and Results—We surveyed the impact of the disaster on the incidence and clinical characteristics of SCUD in Iwate. To perform complete identification of SCUD for 8 weeks before and 40 weeks after the disaster, medical records and death certificates relevant to SCUD were surveyed in the study area. Compared with the previous year's rate, the incidence (per 10 000 person-year) of SCUD for the initial 4 weeks after the disaster (acute phase) was double (33.5 vs 18.9), and thereafter the rate returned to the previous level. Significant relationships were found between weekly numbers of SCUD and seismic activity (intensity, $r=0.43$; $P<0.005$; frequency, $r=0.46$; $P<0.002$). The standardized incidence ratio (SIR) of SCUD in the acute phase was significantly increased compared with that of previous years (1.71, 95% CI 1.33 to 2.16). Increased SIRs were predominantly found in female subjects (1.73, 95% CI 1.22 to 2.37), the elderly (1.73, 95% CI 1.29 to 2.27), and residents living in the tsunami-stricken area (1.83, 95% CI 1.33 to 2.46). In addition, SIRs for weekdays (1.71, 95% CI 1.28 to 2.24) and nights-mornings (2.09, 95% CI 1.48 to 2.86) were amplified.

Conclusions—The present results suggest that the magnitude of a disaster, related stress, and population aging may cause a temporary increase in the incidence of SCUD with amplification of ordinary weekly and circadian variations. (*J Am Heart Assoc*.2014;3:e000798 doi: 10.1161/JAHA.114.000798)

Key Words: disaster • general population • incidence • sudden death

The northeast Japan earthquake and tsunami that occurred on Friday afternoon, March 11, 2011, caused loss of life, destruction, and dislocation on a massive scale. There is a growing body of reports suggesting there is an increased cardiovascular (CV) risk after earthquakes.^{1–7} Large earthquakes induce fear and anxiety without warning in entire

populations throughout the affected geographic area. In addition, some communities along the seacoast are occasionally stricken by a tsunami immediately after earthquakes, and survivors generally sustain damage and aftershocks for several weeks and months. In these settings, several types of CV risk factors, including emotional and physical stressors, may affect inhabitants. However, given the chaos surrounding such devastating disasters, the impact of this type of tragedy on the extent and duration of CV events, including sudden cardiac and unexpected death (SCUD), remains largely unknown. The purpose of the present study was to investigate the effects of a serious disaster that occurred in northeast Japan on the incidence of SCUD in a community-based population.

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Methods

Study Area

The study area selected was the Iwate prefecture in northeast Japan (Figure 1). According to national census data, the adult population (age \geq 20 years) in 2009, 2010, and 2011 was



Figure 1. Map of the Iwate study area. The epicenter is denoted by the bull's eye. The adult population of the area was approximately 280×10^3 , and the elderly population (aged >65 years) was 32% before the disaster.

285 350, 285 556, and 272 440, respectively. The area consisted of 17 municipalities, and the percentage of elderly persons (aged ≥ 65 years) in the area was 32% before the disaster. The proportion of elderly women (aged ≥ 75 years) was 1.7 times higher than that of men of an equivalent age. In the study area, there were 12 general hospitals with emergency departments that were capable of caring for patients with acute events including ambulance transfer. To evaluate the effect of the tsunami on the incidence of SCUD, the area was divided into 2 regions according to the percentage of tsunami flood area per built-up area $<10\%$ and $>10\%$ of each municipality, namely the tsunami flooding area and the control area. There were no significant differences in maximum seismic intensity between the 2 areas (5.0 ± 0.6 in tsunami area vs 4.6 ± 0.4 in control area; NS). The definition of the flooding area and the maximum seismic intensities for each municipality were given in our previous report.⁸ Seismic intensity and frequency of aftershocks within the study area were obtained from the Iwate branch of the Japan Meteorological Agency.

Definition and Case Ascertainment

The definition of SCUD was based on the World Health Organization (WHO) criteria for sudden death.⁹ The criteria define 2 categories as follows: (1) witnessed; death occurring within 1 hour of developing symptoms, and (2) unwitnessed;

death within 24 hours of a subject being seen alive and symptom free. The research information was collected and checked mainly by the following 2 methods. First, the study team visited all referral hospitals in the study area and reviewed clinical files of all patients admitted to the emergency department (cases from January 2009 to December 2011). After a brief discussion with attending physicians, eligible cases were registered with patient information (sex, age, address, time between onset and death, history of cardiovascular disease, symptoms). Second, the 10th revision of the *International Statistical Classification of Diseases and Related Health Problems (ICD-10)* codes (I20 to I25, I46, I49.0, I50, I71, R96, and R98) indicating possible SCUD for all residents who died between January 2009 and December 2011 in these 12 municipalities were obtained from the Ministry of Health and Welfare in Japan with official permission (No. 1126-4). Thereafter, physician-signed death certificates matched by these ICD-10 codes were extracted and carefully reviewed, and eligible cases were registered as SCUD with capture of sex, age, address, time between onset and death, and category of place of death. Use of both of these methods allowed us to be confident that we had identified virtually all SCUD cases admitted to the referral hospitals and those that occurred outside of hospitals (without admission) within the study area. According to the WHO-MONICA (Multinational MONItoring of trends and determinants in CARdiovascular disease) definition,¹⁰ SCUD cases in which the patients complained of chest pain or had a history of coronary artery disease were designated to possible acute myocardial infarction. Subjects with SCUD who were aged <20 years and/or were residents outside the study district were excluded from the study. Cases of death due to external causes and drowning were excluded from the study.

Ethics

Approval was obtained from the ethics review board of Iwate Medical University Institutional Review Board before commencement of the study.

Statistics

The present study compared weekly numbers of SCUD in the study area for 8 weeks before and 40 weeks after the disaster in 2011 with those for 2 nondisaster years (2009 and 2010) as a control. Because the intention was to test whether changes in the incidence of SCUD after the disaster were greater than normal seasonal variation, a lengthy observation period (48 weeks) was chosen. To examine the time-dependent effects on the incidence of SCUD after the disaster, 3 phases were established: namely, the prior phase (the 8 weeks before March 11), the acute phase (the first 4 weeks

after March 11), and the recovering phase (from 5 to 40 weeks after March 11). Rates of SCUD (per 10 000 person-years) for these 3 phases in the disaster year were calculated and were compared with those for the control year. Pearson correlation coefficients were used to examine associations between the weekly number of SCUD cases and the maximum weekly seismic intensity or the weekly frequency of earthquakes (seismic intensity ≥ 1). In addition, to elucidate the demographic and clinical characteristics of SCUD cases, several characteristics relating to sex, age, residence area (tsunami and control areas), and onset time of SCUD (weekday vs weekend/night–morning vs day–evening) were compared with those of the control years. For this analysis, standardized incidence ratios (SIRs) and 95% CIs were calculated. The SIR during the acute phase was determined from the number of observed cases relative to the number of expected cases calculated by age-adjusted incidence rates for 2 nondisaster years (2009–2010). Weekdays and weekend were defined as Monday to Friday and Saturday to Sunday, respectively. The day time-band was divided into 2 categories, namely night–morning zone (11 PM to 10 AM) and day–evening zone (11 AM to 10 PM). A significant difference was defined as $P < 0.05$.

Results

The total number of SCUD cases in the study area during the 3 years was 1246 ($n=398$ in 2009, $n=417$ in 2010, $n=431$ in 2011). Of these, 48% of cases were checked and registered by review of their clinical files. Of these 1246 cases, 57% were recorded as having died within 1 hour after the onset of symptoms (witnessed SCUD). The remaining 43% of cases were unwitnessed SCUD but were adjudged to be alive at least 24 hours before onset. These were confirmed by physician-signed death certificates that were generally drawn up according to verbal information from the patients' family members or neighbors, status of rigor mortis, and rectal temperature. According to the WHO-MONICA criteria, 16% of cases were designated as possible acute myocardial infarction due to a history of coronary artery disease or having chest pain just before the death. The number of deaths by ICD-10 code groupings were follows: 279 cases in I20 to I25, 606 cases in I46 and I49, 209 cases in I50, 50 cases in I96 and I98, and 102 cases in the other categories.

The secular trend in actual numbers of SCUD per week in the control year (mean of 2009 and 2010) and the disaster year (2011) is shown in Figure 2. The average number during the prior phase (8 weeks before March 11) was similar between the control year and the disaster year (9.7 vs 8.9 per week). In contrast, after the disaster on March 11, 2011, the number during the first week increased suddenly to 24 per week and remained high during the following 4 weeks.

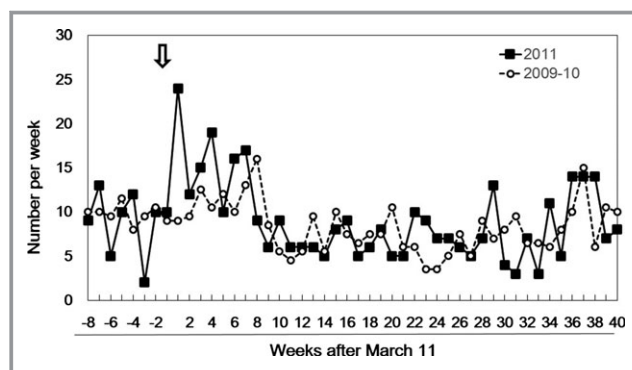


Figure 2. Secular trend in weekly numbers of SCUD cases before (mean for 2009 and 2010) and after the disaster (2011) in the study area. The day of the disaster is shown by the arrow. SCUD indicates sudden cardiac and unexpected death.

Thereafter, however, the number decreased promptly and paralleled the number of the control year until the 40th week after March 11. The overcompensated decrease after the initial increase was not observed during the recovering phase.

The crude incidence per 10 000 person-years is shown in Figure 3 (left). The incidence was similar in the prior phase (17.8 in the control year vs 17.0 in the disaster year). For the acute phase, the rate in the disaster year was approximately twice that in the control year (33.5 vs 18.9). However, in the recovering phase, the incidence was similar between the disaster year and the control year (14.6 vs 15.4). When the analysis was limited to SCUD cases occurring within 1 hour of onset (witnessed SCUD), similar trends were found (prior phase, 10.9 vs 10.7; acute phase, 9.8 vs 19.6; recovering phase, 8.1 vs 9.0; Figure 3 [right]).

The weekly number of SCUD in the disaster year was significantly correlated with the weekly maximum seismic intensity ($r=0.43$, $P < 0.005$; Figure 4 [left]) and with the frequency of quakes ($r=0.46$, $P < 0.002$; Figure 4 [right]). When this analysis was limited to cases within the prior and acute phases (12 weeks), the significance remained robust (vs intensity; $r=0.78$, $P < 0.05$; vs frequency; $r=0.75$, $P < 0.05$).

The mean age of patients with SCUD in the acute phase did not differ significantly between the disaster year and the control year (80 ± 10 vs 78 ± 14 ; NS). The percentage of women in the acute phase corresponding period also did not differ significantly compared with the control year (47% vs 44%; NS). The SIRs of SCUD during the acute phase were compared in terms of sex, age groups, residence areas, day of the week, and time zone of the day and are shown in the Table. As a whole, the rate during the acute phase was nearly doubled (1.71, 95% CI 1.33 to 2.16). This increase was predominantly found in women (1.73, 95% CI 1.22 to 2.37), and subjects aged >75 years (1.73, 95% CI 1.29 to 2.27). Although the rise was significant in the area severely damaged by the tsunami (1.83, 95% CI 1.33 to 2.46), the

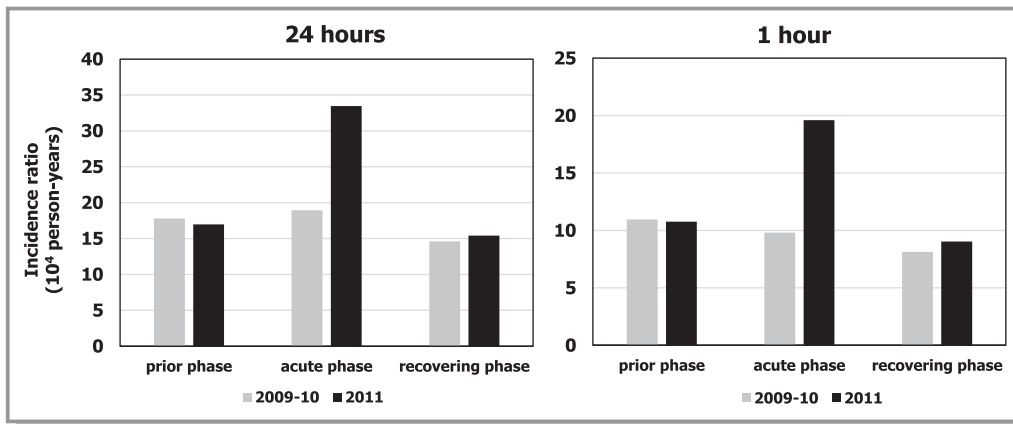


Figure 3. Comparison of incidence (per 10 000 person-years) of SCUD cases before (2009–2010) and after (2011) the disaster in 3 phases (prior phase, 8 weeks before March 11; acute phase, the first 4 weeks after March 11; recovering phase, from 5 to 40 weeks after March 11). Left: Incidence of SCUD occurring within 24 hours after onset. Right: Incidence of SCUD occurring within 1 hour after onset. SCUD indicates sudden cardiac and unexpected death.

increase was borderline in the control area (1.53, 95% CI 0.99 to 2.24). When day of the week was divided into weekday and weekend, the increase in the SIR was significant only for weekdays (1.71, 95% CI 1.28 to 2.24). In addition, when the SIR of SCUD was compared between the 2 time zones, a significant increase was observed for the night-morning classification only (2.09, 95% CI 1.48 to 2.86).

the tsunami flood area. After the disaster, the incidence of SCUD was enhanced on weekdays and during the night-morning time zone. Moreover, the present study has shown that the increased incidence observed during the acute phase fell promptly to the control year level without overcompensation and remained unchanged for at least 9 months until the end of 2011.

Discussion

The present study has demonstrated for the first time that the population-based incidence of SCUD during a 4-week period after a huge natural disaster (earthquake and tsunami) was approximately twice that seen during a corresponding control year. This increase was related to seismic activity and was found predominantly in women, the elderly, and residents of

Comparison to Previous Studies

Population-based studies examining changes in the incidence of SCUD related to catastrophic natural disasters are limited. Leor et al reported that the number of sudden deaths occurring outside hospitals was increased 5-fold on the day of an earthquake compared with the preceding week.¹¹ Their study also suggested that there was a rebound decrease

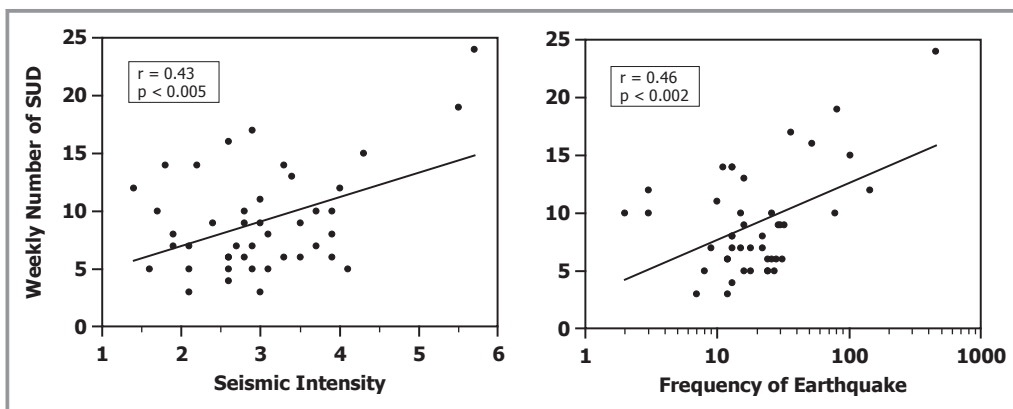


Figure 4. Scatter diagrams and regression lines between number of SCUD cases and seismic intensity (left) or seismic frequency (right) during the study period in 2011. SCUD indicates sudden cardiac and unexpected death.

Table. Standardized Incidence Ratio (SIR) and Number of SCUD Cases for the Acute Phase in 2011 Compared With the Corresponding Period in 2009–2010

	Observed Number	Expected Number*	SIR	Lower 95% CI	Upper 95% CI	P Values
All	70	41	1.71	1.33	2.16	<0.001
Sex						
Male	32	20	1.60	1.09	2.26	<0.05
Female	38	21	1.73	1.22	2.37	<0.01
Age						
<75 y	18	11	1.64	0.97	2.59	NS
≥75 y	52	30	1.73	1.29	2.27	<0.001
Area						
Control	26	17	1.53	0.99	2.24	<0.05
Tsunami	44	24	1.83	1.33	2.46	<0.001
Week						
Weekday	53	31	1.71	1.28	2.24	<0.01
Weekend	17	10	1.70	0.99	2.72	<0.05
Time [†]						
Day–evening	23	20	1.17	0.74	1.75	NS
Night–morning	38	18	2.09	1.48	2.86	<0.001

The SIRs are stratified by several parameters namely sex, age, living area, day of the week, and time zone of the day. SCUD indicates sudden cardiac and unexpected death.

*Expected number was calculated by age-adjusted incidence rates for 2 nondisaster years (2009–2010).

[†]Exact time of death was uncertain in 9% of the subjects.

(overcompensation) in the number of events after this abrupt increase. However, population-based studies examining the temporal impact of natural disasters on the onset of SCUD are scarce. One previous study based on death certificate review showed that the number of cardiac deaths doubled on the day of the disaster and suggested a relationship between the prevalence of cardiac death and the distance from the epicenter in the 1994 Northridge earthquake.³ In the present study, the incidence of SCUD doubled rapidly, and this elevation was sustained for several weeks without an overcompensated decrease. This trend may agree with a previous small study suggesting a persistent increase in the incidence of coronary death after the Hansin-Awaji earthquake.⁵ However, the reason for the difference between the sustained increase in SCUD seen in the present study and the short-term increase with overcompensation observed in the Los Angeles report remains unknown. It may simply be that the magnitude and type of the present earthquake differ from those of the previous study. In the 1994 Northridge earthquake, a magnitude 6.4 main shock was followed by a sequence of aftershocks (eg, 8 of magnitude ≥5 and 48 of magnitude ≥4) lasting for 8 months after the main shock. In the present case, the main shock was magnitude 9.0 and was followed by numerous high-energy aftershocks, specifically 406 of magnitude ≥5 over a period of at least 9 months until

the end of 2011. In fact, the present study showed that SCUD rates were significantly correlated with seismic activity (Figure 4). In addition, a devastating tsunami followed the main shock and destroyed several communities along the seacoast. As a consequence, countless people would have lost family, friends, employees, and businesses, acting as a trigger for serious psychological stress. Furthermore, many people, especially those living in the tsunami devastated area, were compelled to dispose of debris and to take refuge in temporary shelters in freezing temperatures. They were also subject to lifeline damage, lack of daily necessities, and insufficient medical services for several weeks. These sudden and drastic changes in their living conditions along with serious and sustained emotional and physical stressors may be an important cause underlying the prolonged increase in SCUD.

Possible Causes

The true cause for the incidence of SCUD observed in the present study is uncertain. Based on the WHO-MONICA epidemiological definition,¹⁰ only 16% of SCUD cases in this study were designated as acute myocardial infarction due to a history of coronary artery disease and/or complaint of chest pain before death. It is likely that more patients may have

been designated as having acute coronary events because their clinical data and symptoms could not be recognized on the basis of death certificates only. In fact, several hospital-based studies have reported an increase in the number of patients with acute myocardial infarction after an earthquake.^{1,2,4,12} Alternatively, because the prevalence of coronary heart disease in the Japanese population is lower than that of other ethnic populations, several types of CV disease other than coronary artery disease, such as stroke, apical ballooning cardiomyopathy (Takotsubo), primary lethal arrhythmias, and massive pulmonary embolism, may be responsible for SCUD observed in the present study. In fact, our separate population-based study has demonstrated that the incidence of ischemic stroke increased significantly for several weeks after the 2011 disaster.¹³ In the case of the 2004 Niigata Prefecture earthquake, the number of patients with apical ballooning cardiomyopathy was reported as increasing without significant changes in the prevalence of acute coronary syndrome.⁶ This type of cardiomyopathy has been suggested as an important cause of sudden death and malignant arrhythmia.¹⁴ In the 4-week period after the same earthquake, Watanabe et al reported a clear increase in cases of pulmonary thromboembolism, and this event was posited as playing a possible pathophysiological role in sudden death among disaster refugees.¹⁵ Because systemic blood pressure levels have been shown to be elevated after earthquakes in hypertensive subjects,^{16,17} hypertension-induced CV events such as acute aortic dissection and aortic aneurysmal rupture may also be causes of SCUD.

Clinical Characteristics

In the present study, we found a pronounced increase in the incidence of SCUD after the earthquake and tsunami among elderly women. Although no population-based studies have undertaken a sex- and age-stratified analysis of the incidence of sudden death after a natural disaster, several previous studies have reported a greater increase among men in the incidence of acute myocardial infarction in urban areas after earthquakes.^{1,3} However, one report conducted in a rural island population demonstrated that the proportion of female patients with acute myocardial infarction increased from 30% to >50% after the 1995 Hanshin-Awaji earthquake.⁴ Our observed increase in the prevalence of SCUD among elderly women may accord with an epidemiological fact that the incidence of sudden death among women aged >75 is comparable to or higher than that in men aged <75.¹⁸ In fact, the number of women aged >75 years in the present study area is 1.7 times higher than that of men in the study area. The mechanisms underlying sudden death in elderly women remain unclear on the basis of our findings, although women are likely to experience ischemia and microvascular disease

without any evidence of obstructive coronary artery disease.¹⁹ Wittstein et al reported on a series of patients showing profound myocardial stunning without obstructive coronary artery disease after acute emotional stress; these patients were mostly female and showed exaggerated sympathetic nervous activity.²⁰

After a disaster, there may be changes in the incidence of SCUD depending on day of the week (weekday vs weekend) and the time of day (night–morning vs day–evening). Several previous studies have reported both weekly and circadian variations in the occurrence of sudden cardiac death. Incidence tends to peak during morning hours and on Mondays.^{21–23} Although the present disaster occurred on a Friday afternoon, which seems to be a less vulnerable time for the onset of events, an increase in SCUD incidence was evident, and this was augmented in particular during night–morning hours and on weekdays. These observations suggest that certain disaster-related factors may augment pathophysiological mechanisms responsible for weekly and circadian variations in the onset of SCUD. It has been suggested that these variations are due to the morning increase in blood pressure, heart rate, vascular tone, blood viscosity, and platelet aggregability and to the psychological stress on Mondays caused by a return to daily activities from days off^{24,25} or general septadian biological rhythm observed in elderly population.^{26,27} In fact, some of these factors were reported to be enhanced after huge earthquakes.^{17,28,29}

Limitations

There are several potential limitations in our study. First, the definition of sudden death in the literature varied, which has made comparability between studies difficult. Several prior studies proposed that sudden unexpected death be defined as a natural, unexpected fatal event occurring within 1 hour of the beginning of symptoms.^{18,30} However, the WHO criteria define sudden cardiac death as sudden unexpected death either within 1 hour of symptom onset (witnessed), or within 24 hours of the subject having been observed alive and symptom free (unwitnessed). The present study applied the WHO criteria and examined the 2 categories separately. The principal findings remain consistent regardless of the definition used, as shown in Figure 3. Second, the incidence of SCUD was determined from an official population census, which was based on resident registration data and may have failed to recognize undeclared migration to remote municipalities. Third, identification of sudden death cases may be difficult under the circumstances of a disaster of this magnitude. In fact, approximately 6000 people (5% of the population) living along the shore drowned or were missing on the day of the tsunami. Of these victims, some may have died

suddenly due to internal causes such as CV disease before being swept away by the flood. They may thus have been misclassified as death by drowning or external cause. These 2 possibilities may have led to an underestimation of the incidence of SCUD within the tsunami area. Fourth, because few cases underwent autopsy due to the state of chaos after the disaster, half of the present SCUD cases were registered by death certificate information only, without detailed pathological or clinical information. Several previous studies have suggested that many “unexplained” deaths may be due to heritable or other identifiable causes if detailed post-mortem examinations using autopsy and molecular biology examination are conducted.^{31,32} It is therefore inevitable that the exact causes of SUD remain unknown. Finally, given that the study looked at the number of SCUD in the year-long period (Figure 2), there may be a nonuniform distribution in the weekly number of SCUD cases during the control year. This means that seasonal variation and unknown chronobiological factors may modify the true effects of the disaster on the incidence of SCUD.

Conclusions

The population-based incidence of SCUD nearly doubled after the huge natural disaster due to the earthquake and tsunami. This increase was related to seismic activity and was found predominantly in women, the elderly, and residents of the tsunami flood area. After the disaster, the incidence of SCUD was enhanced on weekdays and during the night-morning time zone. These results suggest that the magnitude of a disaster, related stress, and population aging may cause a temporary increase in the incidence of SCUD with amplification of ordinary weekly and circadian variations.

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Disclosures

None.

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