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Evacuation is a Risk Factor for the Development of Diabetes among Evacuees from the Great East Japan Earthquake: A 4-Year Follow-Up Study of the Fukushima Health Management Survey

Running title: Evacuation is a Risk Factor for Diabetes Onset

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Introduction

The Great East Japan Earthquake occurred on March 11, 2011. After the earthquake, a massive tsunami hit the Tokyo Electric Power Company's Fukushima Daiichi Nuclear Power Plant in Fukushima Prefecture, causing the release of radiation. The Fukushima Daiichi nuclear disaster forced evacuation from a number of towns and led to lifestyle changes and anxiety over radiation among the evacuees. Immediately after the disaster, the Fukushima Health Management Survey (FHMS) was stared to investigate the effects of long-term exposure to low-dose radiation [1].

Based on data from the comprehensive health check for around 1.6 years follow-up, we previously reported that evacuation is a cause of body weight gain [2], diabetes [3], hypo-high-density lipoprotein (hypo-HDL)-cholesterolemia [4], hypertension [5], and metabolic syndrome [6]. Those results suggested that evacuation may be a risk factor for the development of various disorders.

In our previous study [3], after adjusting for age, gender, body mass index (BMI), smoking status, systolic blood pressure, and HDL-Cholesterol (HDL-C), alanine aminotransferase (ALT), and γ-glutamyl transpeptidase (γ-GT) levels using Cox proportional hazards model, we demonstrated that evacuation was associated with a significantly higher incidence of diabetes. Although it was unclear why evacuation was a risk factor for the development of diabetes, we assumed that the reason could be the associated change in lifestyle. A change in lifestyle is a well-known cause of obesity and can lead to an increase in the incidence of diabetes.

Therefore, the present study concentrated more on lifestyle factors at baseline to see whether they confound the relation between incident diabetes and evacuation and it follows people over a longer time span, four years. And we used the data in the aftermath of the disaster as baseline.

Methods

***Study Population and Design*:** The FHMS was carried out by Fukushima Medical University. The participants were Japanese adults living near the Fukushima Daiichi nuclear power plant in Fukushima Prefecture and residents of Tamura city, Minamisoma city, Kawamata town, Hirono town, Naraha town, Tomioka town, Kawauchi village, Okuma town, Futaba town, Namie town, Katsurao village, Iitate village, and Date city. According to census data from 2010, the populations of these communities were 278,286. In 2008, the Japanese government had started an annual health check program focused on detecting metabolic syndromes in adults aged 40–74 years known as "The Specific Health Check and Guidance System", which was run by the National Health Care Insurers. We followed the dates of annual health checkups from 2011 as a part of a Comprehensive Health Check in the FHMS. A previous report details the methods of the comprehensive health checks and the FHMS [1]. Based on data from the 2010 national census, the target population of adults aged 40–74 years in these 13 municipalities was 125,987 in 2010, a year before the disaster. We obtained the data of 21,354 adults who had undergone an annual health checkup in 2011 after the disaster (baseline) and at least one checkup data in between 2012 and 2014, which represented about 17% of the population according to the 2010 national census. To conduct a longitudinal analysis, we excluded 3,001 participants who had not received another annual checkup between 2012 and 2014. We also excluded 1,989 participants who had been diagnosed with diabetes in 2011 checkups, and 2,877 participants because of missing data, such as physical activity (2,798 participants), weight change from age 20 years (46 participants), weight change within 1 year (24 participants) and restorative sleep (9 participants) as a baseline. Finally, 13,487 participants underwent follow-up examinations and were included in the analysis (Supplemental Figure 1). If

people participated in the checkups more than once during the survey period, we used the date on which diabetes was identified or the latest date of non-diabetes subjects.

***Ethics Statement*:** Informed consent was obtained from all subjects and community representatives to conduct an epidemiologic study based on the guidelines of the Council for International Organizations of Medical Science [7]. This study protocol was reviewed and approved by the Ethics Committee of Fukushima Medical University (#1916). The study was conducted in accordance with the approved guidelines.

Measurements: The detailed measurements were described in the supplemental information.

***Statistical Analysis*:** The participants were divided into two groups based on residence status after the Great East Japan Earthquake: evacuees (n = 4,235) and non-evacuees (n = 9,252). The baseline characteristics of the participants who received follow-up health examinations were compared between evacuees and non-evacuees using a chi-square test, or Wilcoxon rank-sum test. To evaluate the impact of evacuation on the incidence of diabetes, hazard ratios (HRs) of new onset diabetes and 95% CIs for evacuation were calculated using multivariable-adjusted HRs with adjustment for other potential confounding factors (age, gender, BMI, current smoker, excess alcohol consumption, weight change (≥ 10 kg) from age 20 years, weight change (≥ 3 kg) within 1 year, sleep quality, and physical activity). SAS version 9.3 (SAS Institute, Cary, NC, USA) was used for all analyses. All probability values for statistical tests were 2-tailed, and P values < 0.05 were considered statistically significant.

Results

Baseline Characteristics of Evacuees and Non-Evacuees Who Received Follow-Up Health Examinations after the Disaster

Among all 18,353 participants, including those with diabetes (1,989 participants), the prevalence of diabetes at baseline was estimated to be 10.8% (Supplemental Figure 1). We followed 13,487 participants (43.5% men) without diabetes based on data from annual checkups in 2010–2011 and those who underwent at least one other annual checkup from 2012–2014 (Supplemental Figure 1). Table 1 shows the clinical characteristics of the two groups (evacuees or non-evacuees) at baseline. First, we compared risk factors for the development of diabetes. The evacuees were significantly younger and more frequently female than the non-evacuees. However, the evacuees had significantly higher prevalence of obesity, dyslipidemia, Weight change (≥ 10 kg) from age 20 years, Weight change (≥ 3 kg) within 1 year, adequate sleep, and smoking habit than non-evacuees. No significant differences were observed in HbA1c levels, hypertension, or physical activity between the two groups.

Incidence of Diabetes

Next, we investigated the incidence of diabetes. The cumulative incidence of diabetes was 4.54% (612 participants) over a mean follow-up period of 2.67 years. The total incidence of diabetes was 17.0/1,000 person-years, and that of evacuees was 1.61-fold higher (23.2/1,000-person-years) than that of non-evacuees (14.4/1,000-person-years). Significant differences were observed in baseline characteristics between the two groups, so we applied Cox proportional hazards models. Evacuation was a significant risk factor for the development of diabetes compared with non-evacuation, with a crude HR of 1.73 (95% CI: 1.47–2.04). The age-gender-adjusted HR

for evacuation was 1.78 (95% CI: 1.51–2.09). Furthermore, after full adjustment, the multivariate HR for evacuation was 1.51 (95% CI: 1.28–1.79).

Discussion

We previously demonstrated that after adjusting for age, gender, BMI, smoking status, systolic blood pressure, and HDL-C, ALT, and γ-GT levels [3], evacuation was significantly associated with an increased incidence of diabetes. However, there were several limitations to our previous analysis. First, our previous results were obtained from a short-term follow-up period of only 1.6 years. Second, our previous analysis did not adjust for lifestyle factors such as weight change, physical activity, and sleep quality. Therefore, in the present study, we investigated the effect of prolonged evacuation on the incidence of diabetes after adjusting for these and other lifestyle factors. The results revealed that evacuation after the disaster was an independent risk factor for the development of diabetes, even after adjusting for various lifestyle factors.

Our data show that metabolic factors, including obesity and dyslipidemia, adversely affected evacuees. In addition, the ratios of weight change from age 20 years, sleep deprivation, and current smoking were significantly higher in evacuees than in non-evacuees. Therefore, the disaster was more likely to have a negative effect on the metabolic laboratory test results of evacuees compared with non-evacuees. These findings suggest that chronic metabolic health problems such as obesity, type 2 diabetes, hypertension and dyslipidemia should be carefully monitored and treated after a disaster, especially among evacuees. Living as an evacuee in unfavorable conditions increases stress in terms of privacy, availability of food, duty assignments, income, jobs and health [8]. Particularly in diabetic patients, mental stress can aggravate diabetes control [8, 9]. Although the worsening of glycemic control after disasters may be affected by numerous factors, such as a change in diet, reduction in exercise, and psychological stress, the association between evacuation and the increased incidence of diabetes remains unclear. In a previous report on mental health care, the FHMS revealed that evacuees who believed that radiation exposure causes negative health

effects were significantly more likely to be psychologically distressed [10]. Moreover, psychological distress was significantly more prevalent among residents of evacuation zones, even after adjusting for other significant risk factors such as age, gender, living arrangement, experiencing the nuclear power plant accident, loss of a family member, becoming unemployed, and a history of mental illness. In addition, psychological distress in each evacuation zone was positively associated with the radiation levels in the evacuees' environment [11]. These reports suggest that fear of radiation risk, as well as socioeconomic factors, contribute to psychological distress among evacuees. Although it was not conducted under natural disaster conditions, a prospective population-based study in Finland showed that high psychological distress at baseline predicts the development of metabolic syndrome, independent of age, gender, marital status, educational attainment and baseline health behaviors such as smoking, alcohol intake, and leisure time physical activity [12]. The FHMS showed that evacuation was significantly associated with an increased incidence of metabolic syndrome [6]. Moreover, the same survey also revealed that evacuation was a significant risk factor for overweight [2] and hypertension [5]. Therefore, evacuees tend to be more psychologically distressed and at higher risk of developing metabolic disorders than non-evacuees.

In conclusion, the findings of the present study suggest that prolonged evacuation is a risk factor for the development of diabetes after a disaster. Therefore, it is important to follow-up evacuees and recommend lifestyle changes where necessary.

Duality of interest

The authors declare that there is no duality of interest associated with the manuscript.

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Table 1—Baseline characteristics of the evacuees and non-evacuees who received follow-up health examinations after the Great East Japan Earthquake

	Non-evacuees	Evacuees	*P* value[¶]
Number	9,252	4,235	
Gender (% Men)	44.2%	41.9%	<0.001
Age (years)	64.3 ± 7.8	63.1 ± 8.9	<0.001
HbA1c (%)	5.3 ± 0.3	5.3 ± 0.3	0.071
HbA1c (mmol L^{-1})	34.4 ± 3.3	34.4 ± 3.3	0.071
Obesity (%)[†]	26.7	36.0	<0.001
Hypertension (%)[‡]	52.7	51.9	0.374
Dyslipidemia (%)[§]	50.0	56.0	<0.001
Weight change (≥ 10 kg) from age 20 years (%)	31.3	39.6	<0.001
Weight change (≥ 3 kg) within 1 year (%)	19.2	40.1	<0.001
Regular exercise (%)	34.5	34.3	0.847
Adequate sleep (%)	75.1	64.0	<0.001
Current smoker (%)	12.2	15.1	<0.001
Alcohol consumption (%)			
Non-drinker	29.5	33.8	<0.001
Light drinker	51.9	48.2	
Moderate/heavy drinker[‖]	18.6	18.0	

Data were presented as mean ± standard deviation and percentage values for categorical variables.

[†]Obesity was defined as body mass index ≥ 25 kg $m^{2\ -1}$.

[‡]Hypertension was defined as systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg or self-reported use of blood pressure-lowering drugs.

[§]Dyslipidemia was defined as LDL-C level ≥ 140 mg dL^{-1}, triglyceride level ≥ 150 mg dL^{-1}, HDL-C level < 40 mg dL^{-1}, or self-reported use of cholesterol-lowering drugs.

[‖]Moderate/heavy drinker was defined as ethanol intake ≥ 44 g day^{-1}.

[¶]*P* values comparing the evacuee to the non-evacuee group after the earthquake used the chi-square test or Wilcoxon rank-sum test.