

# Impacts of the Great East Japan Earthquake on diabetic patients

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## Keywords

Glycemic control, Natural disaster, Sympathetic activation

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## ABSTRACT

**Aims/Introduction:** We investigated impacts of the Great East Japan Earthquake on diabetic patients and characterized those with disaster-susceptible diabetes.

**Materials and Methods:** We enrolled 497 diabetic patients who had been followed at hospitals in devastated areas. We collected metabolic parameters prospectively, 1 and 3 months after the earthquake, and retrospectively for pre-earthquake time-points. Questionnaire surveys were carried out regarding earthquake-related damage and post-earthquake lifestyle alterations. Available data were analyzed to examine associations with post-earthquake glycosylated hemoglobin alterations.

**Results:** The mean glycosylated hemoglobin level of the participants was not elevated at 1 month, and was significantly decreased at 3 months as compared with the pre-earthquake glycosylated hemoglobin. There were no significant differences in earthquake-related damage or lifestyle alterations between the improved and worsened glycemic control groups according to the data obtained from the questionnaire survey. As reported, fasting serum C-peptide levels were significantly lower in the worsened glycemic control group ( $P < 0.05$ ). Notably, plasma noradrenaline levels were significantly higher in the worsened glycemic control group ( $P < 0.05$ ). Furthermore, at 1 month after the earthquake, the plasma noradrenaline level was significantly higher in the low C-peptide group (fasting serum C-peptide  $< 1.0$  ng/mL) than in the high C-peptide group (fasting serum C-peptide  $\geq 1.0$  ng/mL), but this difference had disappeared by 3 months after the earthquake. These findings show that post-earthquake plasma noradrenaline levels were temporarily increased in the low C-peptide group.

**Conclusions:** Sympathetic nerve activation might be elicited more easily in subjects with lower endogenous insulin secretory capacity, and could be involved in the mechanism underlying post-earthquake worsening of glycemic control.

## INTRODUCTION

In March 2011, the Tohoku district of Japan suffered from a mega-earthquake, the Great East Japan Earthquake, and the region of the Tohoku district facing the Pacific Ocean was struck by a huge tsunami triggered by this earthquake. Miyagi and Fukushima prefectures were extensively damaged by this calamity, and more than 18,000 people died or remain missing and more than 400,000 people had to be evacuated. Furthermore, severe shortages of food and

other daily supplies as a result of transport disruptions occurred after the earthquake.

Previous reports have shown that, after natural disasters, glycemic control of diabetic patients deteriorates<sup>1–6</sup>. However, when we treated a large diabetic outpatient population affected by the Great East Japan Earthquake, we noticed that alterations of glycemic control after the earthquake varied markedly among patients. To identify the population of diabetic patients whose glycemic control is vulnerable in the aftermath of a natural disaster, we recently carried out a prospective study. We prospectively examined alterations in metabolic parameters including blood glucose, glycosylated hemoglobin (HbA1c),

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bodyweight, clinical systolic blood pressure and fasting serum C-peptide levels, at 1 and 3 months after the Great East Japan Earthquake, in 497 diabetic outpatients treated in hospitals located in devastated areas of Miyagi and Fukushima prefectures. In addition, we carried out questionnaire surveys of the study participants regarding earthquake-related damage and post-earthquake lifestyle alterations, including flooding from the tsunami, damage to homes, evacuation, loss of relatives and alterations in food intake, exercise, alcohol consumption, tobacco smoking, and sleep time, and we analyzed the relationship of each of these items with post-earthquake alterations in glycemic control. By using this Great East Japan Earthquake database, we clarified that post-earthquake worsening of glycemic control correlated strongly with the endogenous insulin secretory capacity of diabetic patients, indicating serum C-peptide levels to be a biological marker predicting those who have disaster-susceptible diabetes<sup>7</sup>. Herein, we further analyzed a large amount of detailed data from the Great East Japan earthquake database to characterize disaster-susceptible diabetic patients with impaired insulin secretory capacity.

## MATERIALS AND METHODS

### Study Population

The present study was approved by the ethics committees of Tohoku University Hospital, Tohoku Pharmaceutical University Hospital, Osaki Citizen Hospital, Minami Tohoku Hospital, South Miyagi Medical Center, Sendai Teisin Hospital, JR Sendai Hospital, Kurihara Central Hospital, Izumi Hospital, Shiogama City Hospital, Saka General Hospital, Kanagami Hospital, Marumori Hospital, Ayashi Heart Clinic, Sendai Red Cross Hospital, Soma Central Hospital and Ohta General Hospital, all of which are located in devastated areas of Miyagi and Fukushima prefectures (Figure 1a). Informed consent was obtained from each participant. The participants of the present study were enrolled from patients who had been followed at the Department of Diabetes and Metabolism in Tohoku University Hospital and the other participating hospitals.

We excluded subjects who were under the age of 20 years at the time of the earthquake, with interruption of hospital visits during the study period and/or who had received treatment for a severe mental disorder. Ultimately, 784 eligible subjects were enrolled. The mean age of these participants was  $65.1 \pm 13.2$  years, and 59.1% were male. We examined parameters in these participants before (the latest time-point during the period from January through March of 2011) 1 month after (from 4 April to 15 April of 2011) and 3 months after (from June through July of 2011) the earthquake. Of these subjects, 287 were excluded due to lack of HbA1c, bodyweight and/or clinical systolic blood pressure data at 1 month and/or 3 months after the earthquake. As a consequence, data from 497 participants including 3.8% of type 1 diabetic patients were available for statistical analysis. The HbA1c levels both before and after the earthquake were available for 492 participants, and bodyweight data both before and after the earthquake were

available for 471. We classified the 497 participants into two groups in which post-earthquake glycemic control showed improvement or worsening as compared with pre-earthquake levels. Participants whose HbA1c values were increased ( $\Delta\text{HbA1c} > 0$ ) and decreased (or were unchanged;  $\Delta\text{HbA1c} \leq 0$ ) at 1 month after the earthquake as compared with pre-earthquake levels were defined as the worsened and improved glycemic control groups, respectively. Among 497 participants, fasting serum C-peptide levels were available for 130 including 14.6% of type 1 diabetic patients. We classified these participants into high and low C-peptide groups according to their fasting serum C-peptide levels (Figure 1b).

### Laboratory and Physical Examinations

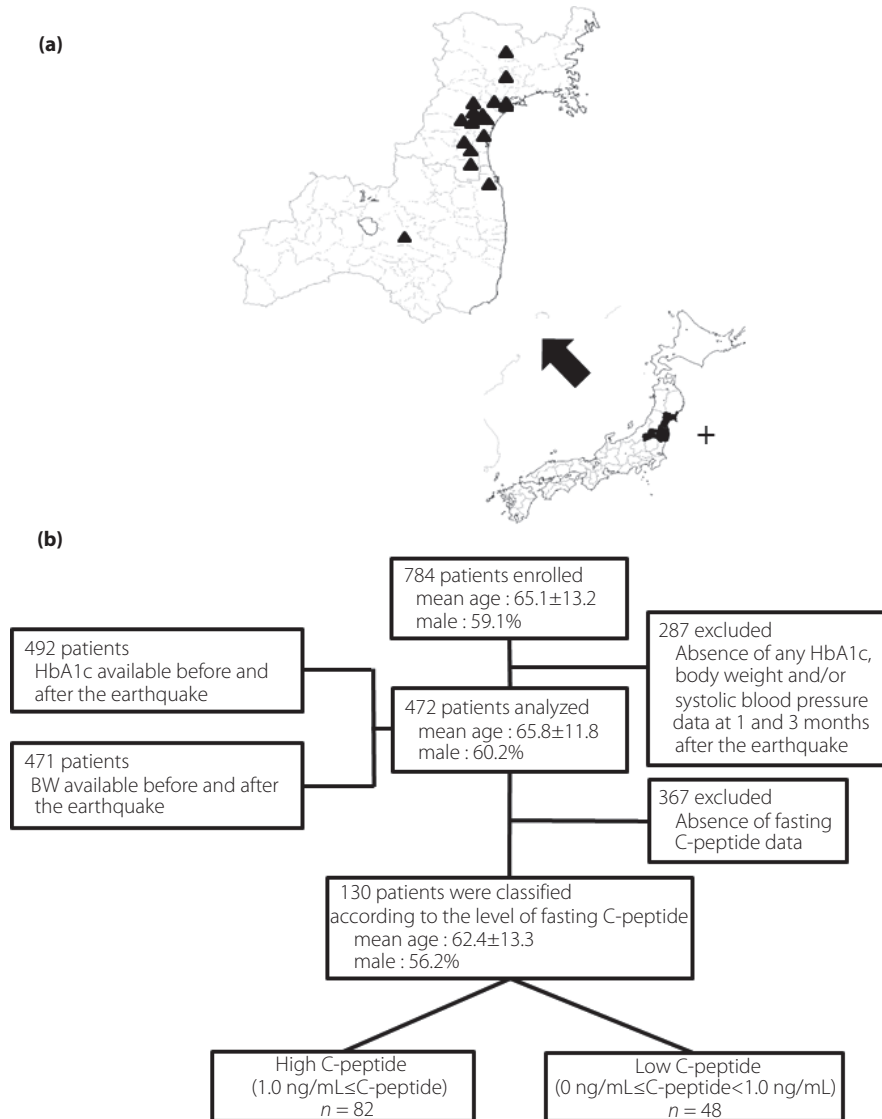
We prospectively monitored HbA1c, bodyweight, clinical systolic blood pressure, several blood parameters including C-peptide, cortisol, catecholamines, hematological values, liver enzymes, lipids, markers of renal functions, uric acid, serum proteins, electrolytes and C-reactive protein, and urinary albumin excretion in these participants at 1 and 3 months after the earthquake, and compared the values obtained with those measured during pre-earthquake periods; that is, at the latest examination time-point during the period from January to March 2011. To compare HbA1c and bodyweight alterations between the pre- and post-earthquake time-points, we retrospectively collected the HbA1c and bodyweight data for pre-earthquake time-points from medical records. HbA1c values were converted from the Japanese Diabetes Society values into National Glycohemoglobin Standardization Program equivalent values.

### Questionnaires

We carried out questionnaire surveys of the study participants regarding earthquake-related damage and post-earthquake lifestyle alterations.

### Statistical Analysis

Continuous variables were expressed as means  $\pm$  standard deviation, and categorical variables were expressed as percentages. Post-earthquake alterations in HbA1c, bodyweight and clinical systolic blood pressure, as compared with pre-earthquake values, were analyzed using Student's *t*-tests. Each parameter was compared between the worsened and improved glycemic control groups using Student's *t*-tests. Each of these parameters was also compared between the high and low C-peptide groups by Student's *t*-tests. We carried out analysis of covariance after adjustment for factors including sex, age and pre-earthquake bodyweight to compare post-earthquake alterations in HbA1c and clinical systolic blood pressure, vs pre-earthquake levels, between the high and low C-peptide groups. The questionnaire results were analyzed using the  $\chi^2$ -test. All statistical analyses were carried out using Statistical Analysis System version 9.3 (SAS Institute Inc., Cary, NC, USA). Differences were considered to be statistically significant at  $P < 0.05$ .



**Figure 1** | (a) Map showing the epicenter of the earthquake and hospitals participating in the present study. +, Epicenter; ▲, hospitals participating in the present study. (b) Study population. HbA1c, glycosylated hemoglobin.

**RESULTS**

**Comparison of Pre- and Post-Earthquake Parameters**

We studied 784 patients followed at hospitals located in devastated areas of Miyagi and Fukushima prefectures. We prospectively monitored HbA1c and bodyweight in these participants at 1 and 3 months after the earthquake, and compared the values obtained with those measured during pre-earthquake periods; that is, at the latest examination time-point during the period from January to March 2011. Of these participants, both HbA1c and bodyweight 1 and 3 months after the earthquake were available in 497 (Figure 1b). Table 1 shows the pre- and post-earthquake parameters examined in these 497 participants. As we collected the pre-earthquake HbA1c and bodyweight data retrospectively, data were lacking for a number of pre-earth-

quake parameters. In particular, the available clinical blood pressure and fasting C-peptide level data before the earthquake were limited. Among all 497 study participants, 60.2% were male and their mean age was  $65.8 \pm 11.8$  years. Of these 497 patients, 464 received medications for diabetes and 330 were receiving medications for hypertension. Unexpectedly, the mean HbA1c level of the participants was not elevated at 1 month, and was significantly decreased at 3 months as compared with the pre-earthquake HbA1c value. Pre-earthquake bodyweight was  $65.9 \pm 14.3$  kg, and showed significant reductions to  $65.3 \pm 14.0$  and  $65.3 \pm 14.2$  kg at 1 and 3 months after the earthquake, respectively. Fasting serum C-peptide levels at 1 and 3 months after the earthquake were available for 130 of the 497 participants (Figure 1b), and were  $1.7 \pm 1.5$  and  $1.7 \pm 1.6$  ng/mL,

**Table 1** | Characteristics of 497 participants before the earthquake, and time-courses of glycosylated hemoglobin, bodyweight, clinical systolic blood pressure and fasting serum C-peptide levels

<i>n</i> = 497	Before the earthquake	One month after the earthquake	Three months after the earthquake
Male (%)	60.2		
Age (years)	65.8 ± 11.8		
HbA1c (%)	7.3 ± 1.1 ( <i>n</i> = 492)	7.3 ± 1.0	7.2 ± 1.0***†
BW (kg)	65.9 ± 14.3 ( <i>n</i> = 471)	65.3 ± 14.0*	65.3 ± 14.2**
Clinical SBP (mmHg)		134.2 ± 15.9	130.3 ± 15.2†
Medication for diabetes (%)	93.6		
Medication for hypertension (%)	66.7		
Fasting serum C-peptide level, ng/mL ( <i>n</i> = 130)		1.7 ± 1.5	1.7 ± 1.6

Data are presented as means ± standard deviation or ratios (%). The paired test was used for analysis of continuous variables. \**P* < 0.05, before vs 1 month after the earthquake. \*\**P* < 0.05, before vs 3 months after the earthquake. †*P* < 0.05, 1 month vs 3 months after the earthquake. BW, bodyweight; SBP, systolic blood pressure.

respectively. Thus, there were no significant alterations in fasting serum C-peptide levels during the study period.

#### Evaluation of Earthquake-Related Damage and Post-Earthquake Lifestyle Alterations

To estimate the impact of the earthquake on our participants, we carried out a questionnaire survey to ascertain earthquake-related damage and post-earthquake lifestyle alterations, followed by analyzing the available responses to each question. To assess earthquake-related damage, we asked questions about flooding from the tsunami, damage to homes, evacuation to refuges and the loss of relatives. As to post-earthquake lifestyle alterations, we asked whether there had been changes in meal quantities, meal compositions, amounts of exercise, amounts of alcohol consumed and tobacco smoking, and sleep time, as well as whether or not drug treatments had been interrupted (Table 2). Of all study participants, 9.8% were exposed to brine from the tsunami, 49.3% experienced damage to their homes including 25.0% with massive damage, 12.2% were forced to

evacuate to places of refuge, 28.9% experienced the loss of relatives and 2.8% lost their jobs. Meal quantities were reported to have decreased by 33.6% of participants, and 40.4% felt that meal compositions had been altered after the earthquake (Table 2). The amount of exercise was decreased for 21.1% of the participants. It should be noted that just 8.6% of the participants had experienced an interruption in their antidiabetes medication regimens in the present study population.

#### Comparison of Questionnaire Items and Metabolic Parameters Between the Improved and Worsened Glycemic Control Groups

Next, to identify factors involved in worsening glycemic control, we divided these participants into two groups; that is, the improved and worsened glycemic control groups, based on changes in HbA1c. We compared earthquake-related damage and lifestyle alterations between these two groups using data collected with the questionnaire. Antidiabetes medication interruption ratios were similar in the two groups of participants.

**Table 2** | Questionnaire results for 497 participants

Flooding from the tsunami, % ( <i>n</i> = 366)	Yes 9.8	No 90.2	
Home loss/damage, % ( <i>n</i> = 349)	Yes 49.3	No 50.7	
	More than half 25.0	Half or less 75.0	
Evacuation to refuge, % ( <i>n</i> = 361)	Yes 12.2	No 87.8	
Loss of relatives, % ( <i>n</i> = 367)	Yes 28.9	No 71.1	
Job loss, % ( <i>n</i> = 357)	Yes 2.8	No 97.2	
Change in meal amount, % ( <i>n</i> = 357)	Increase 5.3	Decrease 33.6	Unchanged 61.1
Change in meal composition, % ( <i>n</i> = 366)	Yes 40.4	None 59.6	
Change in exercise amount, % ( <i>n</i> = 361)	Increase 15.5	Decrease 21.1	Unchanged 63.4
Change in drinking amount, % ( <i>n</i> = 361)	Increase 1.7	Decrease 12.2	Unchanged 31.6
(Non-drinker, <i>n</i> = 197)			
Change in smoking amount, % ( <i>n</i> = 352)	Increase 1.7	Decrease 5.1	Unchanged 14.8
(Non-smoker, <i>n</i> = 276)			
Change in sleep time, % ( <i>n</i> = 361)	Increase 4.4	Decrease 35.2	Unchanged 60.4
Interruption of drug(s), % ( <i>n</i> = 360)	Yes 8.6	None 91.4	

Data are presented as ratios (%).

Unexpectedly, we failed to detect any significant differences in earthquake-related damage or lifestyle alterations between the improved and worsened glycaemic control groups (Table 3).

We also compared other parameters, including sex, age, pre-earthquake HbA1c, pre-earthquake bodyweights, ratios of the participants receiving medications for diabetes and/or hypertension, and blood metabolic parameters, including serum lipids and hormones, at 1 month after the earthquake between the improved and worsened glycaemic control groups (Table 4). As we previously reported<sup>7</sup>, C-peptide levels were significantly lower in the worsened glycaemic control group. Further analysis showed that pre-earthquake bodyweights were significantly lower in the worsened glycaemic control group, which is consistent with the previously documented correlation between low fasting serum C-peptide levels and low bodyweights<sup>8</sup>. Male-to-female ratios, age, and ratios of the participants receiving medications for diabetes and/or hypertension were similar. Importantly, ratios of the participants receiving insulin treatments were also similar in the two groups. Pre-earthquake HbA1c values were significantly higher in the improved glycaemic control group. Notably, plasma noradrenaline levels were significantly higher in the worsened than in the improved glycaemic control group.

#### Characterization of Highly Disaster-Susceptible Diabetic Patients with Impaired Insulin Secretory Capacity

We recently clarified post-earthquake worsening of glycaemic control to correlate strongly with the endogenous insulin secretory capacity of diabetic patients. This finding showed serum C-peptide levels to be a biological marker predicting highly disaster-susceptible diabetic patients<sup>7</sup>. Therefore, to characterize disaster-susceptible diabetic patients with impaired insulin

secretory capacity, we next aimed to examine post-earthquake alterations of several parameters in groups based on their fasting serum C-peptide levels. According to a previous study<sup>9</sup>, we classified 130 participants, whose fasting serum C-peptide levels 1 month after the earthquake were available, into high C-peptide (fasting serum C-peptide level  $\geq 1.0$  ng/mL) and low C-peptide (fasting serum C-peptide level  $< 1.0$  ng/mL) groups (Figure 1b). Mean fasting serum C-peptide levels of the high and low C-peptide groups were  $2.5 \pm 1.4$  and  $0.4 \pm 0.4$  ng/mL, respectively (Table 5). The questionnaire items; that is, earthquake-related damage, including flooding from the tsunami, damage to homes, evacuation to refuges and loss of relatives, and life style alterations, including job loss, altered amounts and compositions of meals, amounts of exercise, alcohol consumption, tobacco smoking, sleep time, and interruption of antidiabetes medication regimens, did not differ significantly between the two groups (Table 5). As we previously reported<sup>7</sup>, post-earthquake glycaemic control in the low C-peptide group showed greater deterioration than that in the high C-peptide group (Table 5). Consistently, glycaemic control of type 1 diabetic patients deteriorated significantly from the pre-earthquake level of 7.8 to 8.2% after the earthquake ( $P = 0.009$ ).

Notably, plasma noradrenaline at 1 month after the earthquake was significantly higher in the low than in the high C-peptide group. In contrast, at 3 months after the earthquake, plasma noradrenaline in the low C-peptide group had decreased to a level similar to that in the high C-peptide group, while fasting C-peptide levels still differed markedly between these two groups (Table 5). Thus, plasma noradrenaline levels were temporarily increased in the low C-peptide group. These findings suggest that patients with impaired insulin secretory capacity are prone to sympathetic activation,

**Table 3** | Questionnaire results for the improved and worsened glycaemic control groups

	$\Delta\text{HbA1c} \leq 0$	$\Delta\text{HbA1c} > 0$	<i>P</i>
<i>n</i>	290	207	
Flooding from the tsunami, % ( <i>n</i> = 366)	11.4	7.5	0.3
Home loss/damage (over half), % ( <i>n</i> = 349)	13.5	10.6	0.5
Evacuation to refuge, % ( <i>n</i> = 361)	12.1	12.3	1.0
Loss of relatives, % ( <i>n</i> = 367)	27.4	31.1	0.5
Job loss, % ( <i>n</i> = 357)	4.1	0.7	0.1
Reduction of meal amount, % ( <i>n</i> = 357)	30.2	38.7	0.1
Change in meal composition, % ( <i>n</i> = 366)	39.7	41.5	0.7
Reduction of exercise, % ( <i>n</i> = 361)	21.3	20.7	1.0
Reduction of alcohol consumption, % ( <i>n</i> = 361) (Non-drinker, <i>n</i> = 197)	12.7	11.5	0.9
Reduction of smoking, % ( <i>n</i> = 352) (Non-smoker, <i>n</i> = 276)	4.3	6.3	0.5
Reduction of sleep time, % ( <i>n</i> = 361)	36.5	33.1	0.6
Interruption of drug(s), % ( <i>n</i> = 360)	8.4	9.0	0.9

Data are presented as ratios (%). A  $\chi^2$ -test was applied for analysis of categorical variables.  $\Delta\text{HbA1c}$ , the amount of glycosylated hemoglobin change at 1 month after the earthquake vs before the earthquake;  $\Delta\text{HbA1c} \leq 0$ , improved glycaemic control group;  $\Delta\text{HbA1c} > 0$ , worsened glycaemic control group.

**Table 4** | Comparison of blood and urinary parameters at 1 month after the earthquake between the improved and worsened glycemic control groups

	$\Delta\text{HbA1c} \leq 0$	$\Delta\text{HbA1c} > 0$	<i>P</i>
<i>n</i>	290	207	
Male (%)	60.0	60.4	1.0
Age (years)	65.3 ± 12.4	66.6 ± 11.0	0.2
HbA1c, %† ( <i>n</i> = 492)	7.5 ± 1.1	7.1 ± 1.0	<0.05
Medication for diabetes, % ( <i>n</i> = 496)	93.8	93.2	0.9
Receiving insulin treatments, % ( <i>n</i> = 468)	42.2	42.5	1.0
Medication for hypertension, % ( <i>n</i> = 495)	69.2	63.1	0.2
BW, kg† ( <i>n</i> = 471)	67.5 ± 15.0	63.7 ± 13.0	<0.05
Fasting serum C-peptide level, ng/mL ( <i>n</i> = 130)	2.1 ± 1.6	1.3 ± 1.2	<0.05
Serum cortisol, µg/dL ( <i>n</i> = 102)	9.5 ± 4.0	9.9 ± 3.4	0.6
Plasma adrenaline, ng/mL ( <i>n</i> = 102)	0.04 ± 0.03	0.05 ± 0.03	0.3
Plasma noradrenaline, ng/mL ( <i>n</i> = 102)	0.43 ± 0.15	0.53 ± 0.24	<0.05
Plasma dopamine, ng/mL ( <i>n</i> = 102)	0.02 ± 0.01	0.02 ± 0.01	0.7
White blood cells, 10 <sup>3</sup> /µL ( <i>n</i> = 237)	6.3 ± 1.9	6.0 ± 1.8	0.2
Red blood cells, 10 <sup>6</sup> /µL ( <i>n</i> = 237)	442.4 ± 56.5	436.5 ± 48.3	0.4
Hemoglobin, g/dL ( <i>n</i> = 237)	13.4 ± 1.8	13.4 ± 1.5	1.0
Platelets, 10 <sup>3</sup> /µL ( <i>n</i> = 236)	21.5 ± 7.2	21.4 ± 5.4	0.9
Serum aspartate aminotransferase, U/L ( <i>n</i> = 378)	25.4 ± 12.0	24.6 ± 10.7	0.5
Serum alanine aminotransferase, U/L ( <i>n</i> = 377)	25.8 ± 19.8	24.4 ± 15.7	0.4
Serum γ-glutamyl transpeptidase, IU/L ( <i>n</i> = 336)	41.2 ± 55.2	41.6 ± 68.6	1.0
Serum alkaline phosphatase, U/L ( <i>n</i> = 275)	234.4 ± 99.7	245.7 ± 79.2	0.3
Serum lactate dehydrogenase, U/L ( <i>n</i> = 268)	200.2 ± 41.8	192.1 ± 31.9	0.1
Serum total cholesterol, mg/dL ( <i>n</i> = 393)	183.8 ± 29.7	189.1 ± 33.2	0.1
Serum HDL-cholesterol, mg/dL ( <i>n</i> = 434)	57.3 ± 17.2	58.3 ± 16.3	0.5
Serum LDL-cholesterol, mg/dL ( <i>n</i> = 424)	105.4 ± 26.1	106.3 ± 27.1	0.7
Serum triglyceride, mg/dL ( <i>n</i> = 434)	126.4 ± 69.6	126.8 ± 72.5	0.9
Serum blood urea nitrogen, mg/dL ( <i>n</i> = 368)	15.3 ± 4.9	16.5 ± 6.2	0.1
Serum creatinine, mg/dL ( <i>n</i> = 379)	0.8 ± 0.3	0.8 ± 0.3	0.6
Serum uric acid, mg/dL ( <i>n</i> = 341)	5.2 ± 1.5	5.1 ± 1.4	0.5
Serum total protein, g/dL ( <i>n</i> = 66)	7.3 ± 0.6	7.1 ± 0.5	0.3
Serum albumin, g/dL ( <i>n</i> = 64)	4.1 ± 0.3	3.9 ± 0.5	0.1
Serum sodium, mEq/L ( <i>n</i> = 206)	140.8 ± 2.2	140.4 ± 2.7	0.3
Serum potassium, mEq/L ( <i>n</i> = 208)	4.4 ± 0.5	4.4 ± 0.4	1.0
Serum chloride, mEq/L ( <i>n</i> = 203)	103.4 ± 2.7	103.3 ± 2.7	0.9
Serum C-reactive protein, mg/dL ( <i>n</i> = 22)	0.4 ± 0.4	0.6 ± 0.6	0.2
Urinary albumin excretion, mg/g·cre ( <i>n</i> = 103)	114.6 ± 200.4	62.2 ± 171.5	0.2

Data are presented as means ± standard deviation or ratios (%). Student's *t*-test was used for analysis of continuous variables. A  $\chi^2$ -test was applied for analysis of categorical variables. †Values before the earthquake.  $\Delta\text{HbA1c}$ , the amount of glycosylated hemoglobin change at 1 month after the earthquake vs before the earthquake;  $\Delta\text{HbA1c} \leq 0$ , improved glycemic control group;  $\Delta\text{HbA1c} > 0$ , worsened glycemic control group; BW, body-weight; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

which might be involved in the observed worsening of their glycemic control.

## DISCUSSION

In the present study, unexpectedly, the mean post-earthquake HbA1c value was lower than that measured during the pre-earthquake period in the entire study group of 497 participants (Table 1). Glycemic control of diabetic patients was previously reported to worsen after natural disasters<sup>1–6</sup>. Ogawa *et al.*<sup>10</sup> reported worsening of glycemic control after the Great East Japan Earthquake in 63 patients with diabetes living in coastal

areas. In their study, 44% of the subjects were affected by the tsunami. The loss of medical information as a result of the tsunami, and prescription of less effective medications after the disaster were hypothesized to be factors contributing to the worsening glycemic control in their study. However, when we treated many diabetic outpatients affected by the disaster, we noticed that alterations of glycemic control after the earthquake varied considerably among patients, and that this variation did not always appear to be attributable to these social factors. Therefore, we searched for other possible causes, including both social and biological factors, which might explain the variation

**Table 5** | Comparison of blood and urinary parameters at 1 month after the earthquake between the high and low C-peptide groups

	High C-peptide	Low C-peptide	P
<i>n</i>	82	48	
Male (%)	58.5	52.1	0.6
Age (years)	62.8 ± 12.6	61.8 ± 14.5	0.7
HbA1c, %† ( <i>n</i> = 128)	7.5 ± 1.2	7.6 ± 1.2	0.7
ΔHbA1c*, % 1 month after the earthquake – before the earthquake ( <i>n</i> = 128)	−0.1 ± 0.1	0.1 ± 0.1	<0.05
BW, kg‡ ( <i>n</i> = 115)	71.2 ± 19.9	58.8 ± 12.3	<0.05
Clinical SBP 1 month after earthquake, mmHg ( <i>n</i> = 130)	130.7 ± 14.8	126.8 ± 18.2	0.2
Clinical SBP 3 months after earthquake, mmHg ( <i>n</i> = 130)	130.2 ± 15.0	124.5 ± 18.3	0.1
Δ clinical SBP*, mmHg (1 month after the earthquake – 3 months after the earthquake)	0.9 ± 1.7	2.5 ± 2.2	0.3
Fasting serum C-peptide level 1 month after earthquake, ng/mL ( <i>n</i> = 130)	2.5 ± 1.4	0.4 ± 0.4	<0.05
Fasting serum C-peptide level 3 months after earthquake, ng/mL ( <i>n</i> = 115)	2.4 ± 1.6	0.5 ± 0.5	<0.05
Serum cortisol, μg/dL ( <i>n</i> = 101)	9.7 ± 3.8	9.5 ± 3.5	0.8
Plasma adrenaline 1 month after earthquake, ng/mL ( <i>n</i> = 101)	0.04 ± 0.03	0.05 ± 0.03	0.2
Plasma noradrenaline 1 month after earthquake, ng/mL ( <i>n</i> = 101)	0.45 ± 0.19	0.53 ± 0.22	<0.05
Plasma noradrenaline 3 months after the earthquake, ng/mL ( <i>n</i> = 101)	0.43 ± 0.22	0.47 ± 0.21	0.4
Plasma dopamine, ng/mL ( <i>n</i> = 101)	0.01 ± 0.01	0.02 ± 0.02	0.2
White blood cells, 10 <sup>3</sup> /μL ( <i>n</i> = 73)	7.0 ± 2.1	5.4 ± 1.3	<0.05
Red blood cells, 10 <sup>6</sup> /μL ( <i>n</i> = 73)	430.4 ± 48.8	420.7 ± 35.5	0.4
Hemoglobin, g/dL ( <i>n</i> = 73)	13.3 ± 1.5	13.0 ± 1.6	0.5
Platelets, 10 <sup>3</sup> /μL ( <i>n</i> = 73)	21.7 ± 5.6	20.4 ± 4.9	0.3
Serum aspartate aminotransferase, U/L ( <i>n</i> = 102)	23.3 ± 11.8	24.2 ± 7.9	0.6
Serum alanine aminotransferase, U/L ( <i>n</i> = 101)	26.5 ± 21.4	20.4 ± 8.5	<0.05
Serum γ-glutamyl transpeptidase, IU/L ( <i>n</i> = 84)	37.8 ± 25.7	49.0 ± 103.9	0.6
Serum alkaline phosphatase, U/L ( <i>n</i> = 50)	218.4 ± 53.7	326.4 ± 192.1	<0.05
Serum lactate dehydrogenase, U/L ( <i>n</i> = 52)	195.0 ± 44.2	195.4 ± 37.1	1.0
Serum total cholesterol, mg/dL ( <i>n</i> = 117)	186.8 ± 37.0	193.5 ± 35.1	0.3
Serum HDL-cholesterol, mg/dL ( <i>n</i> = 121)	52.2 ± 12.3	63.7 ± 16.7	<0.05
Serum LDL-cholesterol, mg/dL ( <i>n</i> = 121)	108.2 ± 31.4	105.1 ± 28.9	0.6
Serum triglyceride, mg/dL ( <i>n</i> = 122)	139.9 ± 81.3	106.0 ± 58.5	<0.05
Serum blood urea nitrogen, mg/dL ( <i>n</i> = 104)	15.0 ± 5.4	14.5 ± 4.2	0.7
Serum creatinine, mg/dL ( <i>n</i> = 113)	0.9 ± 0.4	0.7 ± 0.1	<0.05
Serum uric acid, mg/dL ( <i>n</i> = 89)	5.6 ± 1.3	4.8 ± 1.4	<0.05
Serum total protein, g/dL ( <i>n</i> = 29)	7.1 ± 0.4	7.3 ± 0.7	0.4
Serum albumin, g/dL ( <i>n</i> = 29)	3.9 ± 0.4	3.8 ± 0.5	0.4
Serum sodium, mEq/L ( <i>n</i> = 51)	141.3 ± 2.1	140.1 ± 2.8	0.1
Serum potassium, mEq/L ( <i>n</i> = 51)	4.3 ± 0.3	4.2 ± 0.4	0.2
Serum chloride, mEq/L ( <i>n</i> = 51)	104.4 ± 2.8	102.9 ± 2.2	0.1
Serum C-reactive protein, mg/dL ( <i>n</i> = 13)	0.7 ± 0.5	0.3 ± 0.3	0.1
Urinary albumin excretion, mg/g·Cre ( <i>n</i> = 69)	75.4 ± 126.3	46.2 ± 69.9	0.2
Flooding from the tsunami, % ( <i>n</i> = 96)	10.3	7.9	1.0
Home loss/damage (over half), % ( <i>n</i> = 92)	15.1	10.3	0.5
Evacuation to refuge, % ( <i>n</i> = 92)	16.7	10.5	0.5
Loss of relatives, % ( <i>n</i> = 98)	33.9	20.5	0.2
Job loss, % ( <i>n</i> = 95)	6.9	0.0	0.2
Decreased meal quantity, % ( <i>n</i> = 97)	48.3	35.9	0.3
Change in meal composition, % ( <i>n</i> = 98)	55.9	46.2	0.4
Reduced exercise, % ( <i>n</i> = 97)	36.2	18.0	0.1
Reduced alcohol consumption, % ( <i>n</i> = 97)	15.5	7.7	0.4
Non-drinker ( <i>n</i> = 55)			

Table 5 | (Continued)

	High C-peptide	Low C-peptide	<i>P</i>
Reduced smoking, % ( <i>n</i> = 96) Non-smoker ( <i>n</i> = 79)	3.5	2.6	1.0
Reduced sleep time, % ( <i>n</i> = 96)	47.4	41.0	0.7
Interruption of drug(s), % ( <i>n</i> = 96)	12.3	15.4	0.8

Data are presented as means  $\pm$  standard deviation or ratios (%). Student's *t*-test was used for analysis of continuous variables. A  $\chi^2$ -test was applied for analysis of categorical variables. \*Analysis of covariance after adjustment for factors including sex, age and pre-earthquake bodyweight was used for the amount of glycosylated hemoglobin (HbA1c) change at 1 month after the earthquake vs pre-earthquake value ( $\Delta$ HbA1c) and  $\Delta$  clinic systolic blood pressure (SBP) data. †Values before the earthquake.  $\Delta$  clinical SBP, amount of clinic systolic blood pressure change at 1 month after the earthquake vs 3 months after the earthquake. Fasting C-peptide level, fasting C-peptide levels at 1 month after the earthquake; High C-peptide group: fasting C-peptide  $\geq$ 1.0 ng/mL; Low C-peptide group, fasting C-peptide <1.0 ng/mL. BW, bodyweight; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

of glycemic control among afflicted patients. The present study population was widely dispersed throughout the devastated areas, from the coast to the mountains (Figure 1a), and a smaller portion (9.8%) of our participants had suffered from the tsunami than the population described in the previous report<sup>10</sup>. Additionally, antidiabetes medication was interrupted in just 8.6% of our patients, although it was reported that diabetic condition after the Great East Japan Earthquake depended on the interruption rate of antidiabetes medication<sup>11</sup>. The low interruption rate of antidiabetes medication could be one of the causes of the lack of the exacerbation of glycemic control, as a whole, after the earthquake in the present study. Furthermore, in the present study, the bodyweight of the participants was significantly reduced after the earthquake in contrast to the previous reports<sup>2,3</sup>. As reduction of bodyweight usually correlates with improvement of insulin resistance and resultant glycemic control<sup>12–14</sup>, this could have played a role in post-earthquake improvement of glycemic control in the present study. Traffic disturbance arose after the earthquake and the tsunami, thereby severe food shortages were experienced for a few weeks in the devastated areas. Indeed, a report from the Japan Dietetic Association showed that the calorie intake of the victims was one-half to one-third of the recommended calorie intake after the Great East Japan Earthquake (<http://www.dietitian.or.jp/eq/pdf/120301-5.pdf>, written in Japanese). Therefore, food shortage could have been involved in the bodyweight reduction and consequent improvement of glycemic control after the earthquake in the present study. Rather unexpectedly, there were no questionnaire items with statistically significant differences between the improved and worsened glycemic control groups. These characteristics of the present study population could allow us to unravel interactions among complex biological factors, such as fasting C-peptide and noradrenaline levels, which are associated with the vulnerability of glycemic control.

Plasma noradrenaline levels at 1 month after the earthquake were significantly higher in the low C-peptide group than in the high C-peptide group (Table 5), suggesting hyperactivation of the sympathetic nerve system in the former. It is conceivable

that severe damage induced by the Great East Japan Earthquake followed by the massive tsunami would produce psychological stress accompanied by anxiety in affected individuals, leading to activation of the sympathetic nervous system. Plasma noradrenaline levels were reduced at 3 months after the earthquake, suggesting post-earthquake sympathetic nervous system activation to be temporary with reversal to basal status at 3 months after the earthquake. In contrast, fasting serum C-peptide levels remained lower at 3 months after the earthquake in the low C-peptide group, showing that these patients had already had low insulin secretory capacity before the earthquake. Unfortunately, the prevalence of late complications of diabetes was unavailable in the participants of this study, and involvement of diabetic complications, especially that of neuropathy, in plasma noradrenaline levels was unclear. However, considering that there were no detectable differences in earthquake-related damage or lifestyle alterations between the improved and worsened glycemic control groups from the questionnaire survey, patients with low insulin secretory capacity might be subject to sympathetic hyperactivation under stressful circumstances. Alternatively, activated states of the sympathetic nervous system immediately after the disaster might be sustained for more than 1 month in these patients, although the mechanism underlying these effects of impaired insulin secretion on sympathetic activity remains unclear. Sympathetic nervous system activation induces insulin resistance<sup>15–17</sup>, resulting in blood glucose elevation<sup>18,19</sup>. In patients with impaired insulin secretory capacity, this hyperglycemic effect could have a greater impact on blood glucose elevation as a result of decreased compensatory insulin secretion. Therefore, sympathetic nerve activation could have contributed to further worsening of glycemic control in the low C-peptide group.

To further assess whether patients in the low C-peptide group actually showed sympathetic activation, we focused on blood pressure data. It is widely accepted that sympathetic activation induces blood pressure elevation<sup>20,21</sup>, and we previously reported significant elevation of self-measured systolic blood pressure in



the morning at home to be sustained for more than 2 weeks after the earthquake in 142 hypertensive patients affected by the Great East Japan Earthquake<sup>22</sup>. As the data of blood pressure in the morning of the participants in the present study were unavailable, we compared clinical blood pressure levels 1 month after the earthquake with those obtained at 3 months, with the latter being assumed to reflect the pre-earthquake levels. In the low C-peptide group, the mean clinical systolic blood pressure value at 1 month after the earthquake was higher than that at 3 months (Table 5), suggesting temporary elevation of blood pressure. Although the difference did not reach statistical significance because of the marked variability within the clinical blood pressure dataset, these results could support the notion that sympathetic hyperactivation occurred, or that sympathetic activation had been sustained until the subacute period after the disaster, in patients with low insulin secretory capacity.

The autonomic nervous system is involved in regulating glucose and energy metabolism<sup>23,24</sup>. Furthermore, we previously reported that interorgan communications mediated by the autonomic nervous system play critical roles in regulating glucose<sup>25</sup> and energy metabolism<sup>26,27</sup>. These findings have shed light on the significance of the autonomic nerve system in maintaining metabolic homeostasis<sup>28</sup>. The present results further suggest its importance in regulating systemic metabolism in humans, especially in post-disaster states. Metabolic homeostasis in diabetic patients with impaired endogenous insulin secretory capacity might be vulnerable due partly to perturbation of the autonomic nervous system, contributing to further worsening of glycemic control.

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## DISCLOSURE

The authors declare no conflict of interest.

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