Hypo-high-density Lipoprotein Cholesterolemia Caused by Evacuation after the Fukushima Daiichi Nuclear Power Plant Accident: Results from the Fukushima Health Management Survey

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Abstract

Objective The Great East Japan Earthquake and the Fukushima Daiichi nuclear disaster forced the evacuation of residents and led to many changes in the lifestyle of the evacuees. A comprehensive health check was implemented to support the prevention of lifestyle-related disease, and we analyzed changes in lipid metabolism before and after these disasters.

Methods Subjects included Japanese men and women living near the Fukushima Daiichi nuclear power plant in Fukushima Prefecture. Annual health checkups, focusing on metabolic syndromes, were conducted for persons ≥ 40 years of age by the Health Care Insurers.

Results A total of 27,486 subjects underwent a follow-up examination after the disaster, with a mean follow-up of 1.6 years. Following the disaster, the prevalence of hypo-high-density lipoprotein (HDL) cholesterolemia increased significantly from 6.0% to 7.2%. In the hypo-HDL cholesterolemia group, the body mass index (BMI), blood pressure, and LDL-C level increased significantly in men after the disaster. On the other hand, in the normal HDL-C level group, the BMI, blood pressure, glucose and lipid metabolism, and liver function were adversely affected. The decrease in HDL-C was significantly greater in evacuees than non-evacuees in the normal HDL-C level group. Furthermore, a multivariate logistic regression analysis showed that the evacuation was significantly associated with the incidence of hypo-HDL cholesterolemia.

Conclusion This is the first study to evaluate how the evacuation affected the incidence of hypo-HDL cholesterolemia and led to an increase in cardiovascular disease. This information may be important in the follow-up and lifestyle change recommendations for evacuees.

Key words: evacuee, the Great East Japan Earthquake, Fukushima Daiichi nuclear power plant accident, Fukushima Health Management Survey, hypo-high-density lipoprotein cholesterolemia, lifestyle

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Introduction

The Great East Japan Earthquake occurred on March 11th, 2011. Following the earthquake, a tsunami hit the Tokyo Electric Power Company's Fukushima Daiichi nuclear power plant, resulting in a radiation hazard in Fukushima Prefecture. The Fukushima Daiichi nuclear disaster forced the evacuation of a number of towns, causing lifestyle changes and anxiety over the radiation exposure in the evacuees. Shortly after the disaster, Fukushima Prefecture launched the Fukushima Health Management Survey to investigate the effect of long-term low-dose radiation exposure caused by the disaster (1). This survey comprises a basic survey to estimate the individual radiation exposure of residents and four detailed surveys that include a comprehensive health check, thyroid ultrasonography, mental health and lifestyle survey, and survey on pregnant women and nursing mothers (1). The comprehensive health check was implemented to aid the early detection and treatment of disease, as well as the prevention of lifestyle-related diseases including diabetes, hypertension, dyslipidemia, obesity, and cardiovascular diseases.

High-density lipoprotein (HDL) promotes the efflux of cholesterol from foam cells in atherosclerotic lesions (reverse cholesterol transport). Several studies indicate that the antioxidative and anti-inflammatory properties of HDL inhibit atherogenesis (2, 3). A low HDL-C level is associated with an increased incidence of cardiovascular events (4) and cerebrovascular accident (CVA) (5, 6). A low HDL-C level (7) is the most common lipoprotein abnormality among patients with cardiovascular disease (CVD) (8), which is now the leading cause of death worldwide (9). Large-scale protective studies have indicated that each 1 mg/dL increase in HDL-C is associated with a 2-3% decrease in the risk of CVD (10). Furthermore, a low HDL-C level commonly occurs as a result of metabolic syndrome, a cluster of factors such as insulin resistance, obesity, and hypertension, associated with an increased risk of coronary artery disease (10). These reports indicate that a low HDL-C level is one of major risk factors in cardiovascular and cerebrovascular diseases (4-6). The Japan Atherosclerosis Society (JAS) guidelines define an HDL-C level <40 mg/dL to indicate hypo-HDL cholesterolemia (11). In addition, environmental factors such as smoking, alcohol consumption and physical activity can affect the HDL-C level, and this association varies according to gender (12). The question arises as to whether this disaster influenced the HDL-C level in evacuees and non-evacuees, and if there is a significant difference in this relationship.

The primary purposes of the Fukushima Health Management Survey are to monitor the long-term health of residents, promote their future well-being, and determine whether long-term low-dose radiation exposure has health effects. Evacuees from the government-designated evacuation zone were forced to change their lifestyle, diet, exer-

cise, and other personal habits. Some did not receive adequate health checkups and were anxious about their health. The comprehensive health check attempts to review residents' health information, while assessing the incidence of various diseases and improve their health status. We herein used the information obtained from the Fukushima Health Management Survey to identify any changes in lipid metabolism, particularly the HDL-C level, before and after the disaster.

Materials and Methods

Subject and study design

The Fukushima Health Management Survey was carried out by Fukushima Medical University. Subjects included in this study were Japanese men and women living near the Fukushima Daiichi nuclear Power plant in Fukushima prefecture and residents of Tamura City, Minami Soma City, Kawamata Town, Hirono Town, Naraha Town, Tomioka Town, Kawauchi Village, Okuma Town, Futaba Town, Namie Town, Katsurao Village, Iitate Village, and Date City. The census populations of these communities were 42,085, 71,661, 16,065, 5,495, 7,927, 15,854, 3,074, 11,553, 7,171, 21,551, 1,582, 6,584, and 67,684 (total: 278,286) in 2010, respectively. All residents of Hirono Town, Naraha Town, Tomioka Town, Kawauchi Village, Okuma Town, Futaba Town, Namie Town, Katsurao Village, and Iitate Village, and part-time residents of Tamura City, Minami-Soma City, Kawamata Town, and Date City were forced to evacuate their homes due to a government mandate after the disaster. Since 2008, residents ≥40 years of age in these communities have undergone annual health checkups by Health Care Insurers with a focus on metabolic syndromes (the target subjects of checkups was 91,554 in 2010). Between 2008 and 2010, 41,633 subjects (18,745 men and 22,888 women; mean age, 67 years) in the communities of interest participated in the health checkups.

The annual health checkups were conducted between June 2011 and March 2013 as part of the comprehensive health check. Detailed methods of the comprehensive health check have been previously reported (1). In brief, this comprehensive health check performed health examinations for individuals of all ages living in the evacuation zone designated by the government who were officially registered residents at the time of the earthquake. Only residents 40-90 years of age were included in the analyses. A total of 27,486 subjects (12,432 men and 15,054 women; follow-up proportion: 66%) underwent the follow-up examination following the disaster, with a mean follow-up of 1.6 years.

Ethics statement

Informed consent was obtained from the community representatives to conduct an epidemiological study according to the guidelines of the Council for International Organizations of Medical Science (13). The study was approved by

the Fukushima Medical University Institutional Review Board (#1916). Individuals older than 40 years of age were evaluated according to items in the Specific Health Examination, which is based on the Act on Assurance of Medical Care for Elderly People (Act No. 80, 1982). The participants in the Fukushima Health Management Survey provided their written informed consent at the follow-up survey. We obtained informed consent from all participants. To use the data before the disaster, we obtained permission from the community representatives because they have managed the data. To compare the data before and after the disaster, we used the health checkup data managed by each community. The participant consent forms were maintained in locked areas in the Fukushima Health Management Survey. The consent procedure was approved by the Fukushima Medical University Institutional Review Board.

Measurements

The examination included height, weight, abdominal circumference/body mass index (BMI), blood pressure, aspartate aminotransferase (AST), alanine aminotransferase (ALT), γ -glutamyl transpeptidase (γ -GT), triglyceride (TG), HDL-C, low-density lipoprotein cholesterol (LDL-C), hemoglobin A1c (HbA1c), fasting plasma glucose, and urine protein and sugar level measurements. The TG, HDL-C, and LDL-C levels before and after the disaster were measured using the Autoanalyzer JCA-BM8030 (JEOL Ltd.) at the laboratory of the Fukushima Preservative Service Association of Health, except for residents in Futaba Town ($n=758$). Since the trends in the TG, HDL-C, and LDL-C levels before and after the disaster in Futaba were similar to those in other communities, we included the data of Futaba in the analyses. Additional measurements included in the examination were the serum creatinine (Cr) level, estimated glomerular filtration rate (eGFR), uric acid (UA) level, urine testing for occult blood, and peripheral blood count, which included the red blood cell count (RBC), hematocrit (Ht), hemoglobin (Hb), platelet count, and white blood cell count (WBC). The value for HbA1c was estimated using a National Glycohemoglobin Standardization Program equivalent value calculated using the equation $\text{HbA1c (\%)} = 1.019 \times \text{HbA1c (JDS (\%))} + 0.30\%$ (14).

Hypo-HDL cholesterolemia was defined as HDL-C <40 mg/dL in accordance with the JAS guidelines (11). Diabetes was defined in accordance with the Japan Diabetes Society (JDS) guidelines (14): a fasting plasma glucose level ≥ 126 mg/dL (7.0 mmol/L), HbA1c level $\geq 6.5\%$, or the self-reported use of antihyperglycemic drugs.

Statistical analysis

Data are presented as the mean $\pm$ deviation (S.D.). Changes in the data before and after the disaster were compared using the paired Student's *t*-test. An analysis of variance (ANOVA) was used to examine the differences in changes in the variables adjusted for age and sex among the evacuees and non-evacuees. These analyses were also tested after

Figure. Prevalence of hypo-HDL cholesterolemia before and after the Great East Japan Earthquake. Subjects were classified into hypo-HDL cholesterolemia and no hypo-HDL cholesterolemia groups according to the Japan Atherosclerosis Society (JAS) guidelines. Hypo-HDL cholesterolemia was defined as a HDL-C level <40 mg/dL. *: $p<0.0001$

stratifying by the HDL-C status: normal HDL-C level group and hypo-HDL cholesterolemia group at baseline. A multivariate logistic regression analysis was used to test for associations between the evacuation and other potential confounders with the incidence of a low HDL-C level. The fit of the models was evaluated using a residual analysis. The incidence of a low HDL-C level after the earthquake among evacuees and non-evacuees was compared using the Mann-Whitney *U* test or χ^2 test. The SAS version 9.3 software program (SAS Institute, Cary, USA) was used for all analyses. All probability values for statistical tests were 2-tailed and *p* values <0.05 were considered to be statistically significant.

Results

Change in the clinical characteristics after the disaster

There were 27,486 participants (12,432 men and 15,054 women; follow-up rate: 66%; mean follow-up period: 1.6 years) who were officially registered residents at the time of the earthquake and underwent a follow-up examination after the disaster.

The HDL-C levels significantly decreased from 56.2 ± 14.4 mg/dL to 55.1 ± 14.3 mg/dL ($p<0.0001$) and 62.1 ± 14.2 mg/dL to 61.5 ± 14.4 mg/dL ($p<0.0001$) in men and women (27,486 participants; 12,432 men and 15,054 women), respectively, after the disaster. Several lines of evidence suggest that a low HDL-C level is one of major risk factors in cardiovascular and cerebrovascular diseases (4-6). In addition, the JAS guidelines (11) define an HDL-C level of <40 mg/dL to indicate hypo-HDL cholesterolemia. Therefore, the subjects were classified into the normal HDL-C level group and hypo-HDL cholesterolemia group at base-

Table 1. Clinical and Biochemical Characteristics of Subjects Classified by HDL-C Level before and after the Great East Japan Earthquake.

HDL-C < 40 mg/dL						
	Men			Women		
	Before	After	p value	Before	After	p value
Number	1,184			467		
Age (years)	67.6 ± 10.1	69.1 ± 10.0	< 0.0001	67.7 ± 9.3	69.2 ± 9.3	< 0.0001
Body weight (kg)	66.0 ± 9.8	66.5 ± 10.0	< 0.0001	55.5 ± 9.2	55.6 ± 9.4	0.672
BMI (kg/m ²)	24.8 ± 3.0	25.0 ± 3.1	< 0.0001	24.8 ± 3.5	24.9 ± 3.6	0.073
SBP (mmHg)	132.6 ± 16.7	134.6 ± 15.3	< 0.0001	132.5 ± 16.9	132.6 ± 15.6	0.969
DBP (mmHg)	78.0 ± 10.7	79.2 ± 10.1	0.000	76.4 ± 9.8	77.2 ± 9.9	0.123
HbA1c (%)	5.67 ± 0.83	5.69 ± 0.83	0.089	5.59 ± 0.58	5.60 ± 0.70	0.566
HDL-C (mg/dL)	35.6 ± 3.3	38.2 ± 6.3	< 0.0001	36.1 ± 3.0	39.7 ± 6.6	< 0.0001
LDL-C (mg/dL)	113.0 ± 31.1	117.4 ± 32.0	< 0.0001	116.2 ± 31.2	122.9 ± 31.4	< 0.0001
AST (IU/L)	25.9 ± 12.5	26.9 ± 13.1	0.002	24.8 ± 13.1	25.7 ± 11.8	0.097
ALT (IU/L)	24.6 ± 20.2	26.1 ± 17.1	0.015	20.3 ± 15.8	21.7 ± 15.3	0.052
γ-GT (IU/L)	38.3 ± 48.8	39.4 ± 41.5	0.220	25.1 ± 18.6	26.5 ± 23.5	0.025
Smoking habit (%)						
Yes	32.4	26.9	< 0.0001	5.0	3.7	0.070
No	67.6	73.1		95.0	96.3	
Drinking						
Everyday	24.4	23.1	0.122	1.7	0.7	0.495
Sometimes	25.1	24.0		10.0	11.2	
Little	22.5	25.4		30.0	29.0	
Never	28.1	27.5		38.3	59.1	
HDL-C ≥ 40 mg/dL						
	Men			Women		
	Before	After	p value	Before	After	p value
Number	11,248			14,587		
Age (years)	66.8 ± 9.4	68.3 ± 9.4	< 0.0001	65.7 ± 9.4	67.2 ± 9.4	< 0.0001
Body weight (kg)	62.1 ± 9.6	63.0 ± 9.8	< 0.0001	52.6 ± 8.4	53.0 ± 8.7	< 0.0001
BMI (kg/m ²)	23.5 ± 3.0	23.9 ± 3.1	< 0.0001	23.3 ± 3.4	23.6 ± 3.5	< 0.0001
SBP (mmHg)	132.9 ± 16.6	134.6 ± 15.8	< 0.0001	130.5 ± 17.1	132.2 ± 16.3	< 0.0001
DBP (mmHg)	78.4 ± 10.2	79.5 ± 10.1	< 0.0001	75.9 ± 10.2	77.2 ± 9.9	< 0.0001
HbA1c (%)	5.52 ± 0.67	5.55 ± 0.74	< 0.0001	5.50 ± 0.59	5.49 ± 0.60	< 0.0001
HDL-C (mg/dL)	58.3 ± 13.4	56.9 ± 13.7	< 0.0001	62.9 ± 13.7	62.2 ± 14.0	< 0.0001
LDL-C (mg/dL)	116.0 ± 29.4	118.0 ± 30.3	< 0.0001	124.9 ± 29.4	126.3 ± 30.7	< 0.0001
AST (IU/L)	26.6 ± 11.9	27.2 ± 12.5	< 0.0001	23.8 ± 8.9	24.1 ± 9.8	< 0.0001
ALT (IU/L)	22.8 ± 14.3	24.4 ± 16.5	< 0.0001	18.7 ± 11.2	19.6 ± 13.1	< 0.0001
γ-GT (IU/L)	45.3 ± 61.0	47.6 ± 64.4	< 0.0001	23.6 ± 27.1	24.6 ± 24.1	< 0.0001
Smoking habit (%)						
Yes	23.4	20.3	< 0.0001	3.7	3.4	< 0.0001
No	76.7	79.7		96.3	96.6	
Drinking						
Everyday	48.7	47.7	< 0.0001	4.9	4.9	< 0.0001
Sometimes	22.4	21.6		17.1	15.7	
Little	13.8	14.9		29.3	29.8	
Never	15.0	15.8		48.7	49.6	

Data are presented as mean ± S.D.

BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, HbA1c: hemoglobin A1c, HDL-C: high density lipoprotein cholesterol, LDL-C: low density lipoprotein cholesterol, AST: aspartate aminotransferase, ALT: alanine aminotransferase, γ-GT: γ-glutamyl transpeptidase

line. The prevalence of hypo-HDL cholesterolemia before and after the Great East Japan Earthquake is shown in Figure. Following the disaster, the prevalence of hypo-HDL cholesterolemia significantly increased from 6.0% to 7.2% ($p < 0.0001$).

In the hypo-HDL cholesterolemia group (1,651 participants; 1,184 men and 467 women), the HDL-C level significantly increased from 35.6 ± 3.3 mg/dL to 38.2 ± 6.3 mg/dL ($p < 0.0001$) and 36.1 ± 3.0 mg/dL to 39.7 ± 6.6 mg/dL ($p < 0.0001$) in men and women, respectively, after the disaster. In addition, the ratio of smoking habit significantly decreased from 32.4% to 26.9% ($p < 0.0001$) in only men. However, the BMI, blood pressure, AST, and ALT also significantly increased in both men and women after the disaster.

(Table 1). In the normal HDL-C level group (25,835 participants; 11,248 men and 14,587 women), the HDL-C level significantly decreased after the disaster from 58.3 ± 13.4 mg/dL to 56.9 ± 13.7 mg/dL ($p < 0.0001$) and 62.9 ± 13.7 mg/dL to 62.2 ± 14.0 mg/dL ($p < 0.0001$) in men and women, respectively, whereas the ratio of smoking habit significantly decreased from 23.4% to 20.3% ($p < 0.0001$) and 3.7% to 3.4% ($p < 0.0001$) in men and women, respectively. In addition, the BMI, blood pressure, LDL-C, AST, ALT, and γ-GT levels also increased significantly in men and women ($p < 0.0001$ for both) after the disaster.

Table 2. Clinical and Biochemical Characteristics among Non-evacuees and Evacuees before and after the Great East Japan Earthquake.

HDL-C < 40 mg/dL						
Men						
	Evacuees			Non-evacuees		
	Before	After	p value	Before	After	p value
Number	404			780		
Age (years)	66.7 ± 10.3	68.3 ± 10.3	< 0.0001	68.0 ± 9.9	69.5 ± 9.9	< 0.0001
Body weight (kg)	66.7 ± 9.5	68.1 ± 10.0	< 0.0001	65.6 ± 9.9	65.6 ± 9.9	0.527
BMI (kg/m ²)	25.0 ± 2.8	25.6 ± 3.0	< 0.0001	24.7 ± 3.0	24.8 ± 3.0	0.186
SBP (mmHg)	132.4 ± 17.4	135.5 ± 15.4	0.000	132.7 ± 16.3	134.1 ± 15.2	0.012
DBP (mmHg)	77.4 ± 10.4	80.3 ± 9.5	< 0.0001	78.3 ± 10.8	78.7 ± 10.4	0.333
HbA1c (%)	5.73 ± 0.96	5.74 ± 0.80	0.767	5.63 ± 0.75	5.67 ± 0.85	0.058
HDL-C (mg/dL)	35.6 ± 3.5	37.8 ± 6.7	< 0.0001	35.6 ± 3.2	38.4 ± 6.1	< 0.0001
LDL-C (mg/dL)	111.4 ± 33.2	117.7 ± 34.9	< 0.0001	113.7 ± 30.0	117.2 ± 30.4	< 0.0001
AST (IU/L)	27.5 ± 16.8	28.9 ± 16.2	0.024	25.1 ± 9.4	25.9 ± 10.9	0.038
ALT (IU/L)	26.7 ± 17.3	29.8 ± 20.6	0.000	23.6 ± 21.4	24.1 ± 14.6	0.462
γ-GT (IU/L)	42.6 ± 60.1	44.9 ± 52.5	0.267	36.1 ± 41.6	36.6 ± 34.3	0.569
Smoking habit (%)						
Yes	32.0	27.5	< 0.0001	32.6	26.6	< 0.0001
No	68.1	72.5		67.4	73.4	
Drinking						
Everyday	23.1	21.4	0.557	25.0	24.0	0.354
Sometimes	24.4	23.2		25.4	24.4	
Little	20.5	23.4		23.5	26.4	
Never	32.0	32.0		26.2	25.3	
Women						
	Evacuees			Non-evacuees		
	Before	After	p value	Before	After	p value
Number	160			307		
Age (years)	67.1 ± 9.8	68.8 ± 9.8	< 0.0001	68.0 ± 9.0	69.4 ± 9.0	< 0.0001
Body weight (kg)	55.8 ± 10.1	56.0 ± 10.1	0.406	55.4 ± 8.8	55.4 ± 9.0	0.834
BMI (kg/m ²)	24.9 ± 3.7	25.1 ± 3.7	0.043	24.8 ± 3.5	24.8 ± 3.6	0.548
SBP (mmHg)	132.4 ± 17.7	132.0 ± 15.7	0.616	132.6 ± 16.5	133.0 ± 15.5	0.657
DBP (mmHg)	75.6 ± 8.7	77.5 ± 9.4	0.035	76.8 ± 10.3	77.0 ± 10.2	0.680
HbA1c (%)	5.69 ± 0.72	5.74 ± 0.95	0.121	5.54 ± 0.50	5.52 ± 0.52	0.237
HDL-C (mg/dL)	36.3 ± 2.7	40.1 ± 7.5	< 0.0001	36.1 ± 3.1	39.5 ± 6.2	< 0.0001
LDL-C (mg/dL)	117.5 ± 31.2	124.9 ± 31.3	0.002	115.5 ± 31.2	121.9 ± 31.4	0.000
AST (IU/L)	24.3 ± 9.3	26.4 ± 13.9	0.022	25.0 ± 14.6	25.3 ± 10.6	0.663
ALT (IU/L)	20.7 ± 12.8	24.1 ± 18.9	0.006	20.1 ± 17.1	20.4 ± 12.8	0.666
γ-GT (IU/L)	25.0 ± 18.6	28.9 ± 26.0	0.003	25.1 ± 18.6	25.2 ± 22.0	0.800
Smoking habit (%)						
Yes	6.5	5.1	0.500	4.2	2.9	0.219
No	93.5	94.9		95.8	97.1	
Drinking						
Everyday	2.6	0.6		1.3	0.7	
Sometimes	13.7	13.9	0.364	8.1	9.8	0.905
Little	21.6	20.9		34.2	33.2	
Never	62.1	64.6		56.4	56.4	

Change in the clinical characteristics among non-evacuees and evacuees after the disaster

Next, the effects of the evacuation on lipid metabolism were examined. Among the men (12,432 participants; 4,275 evacuees and 8,157 non-evacuees), the HDL-C levels significantly decreased from 56.7±14.6 mg/dL to 54.2±14.0 mg/dL ($p<0.0001$) and 55.9±14.3 mg/dL to 55.6±14.4 mg/dL ($p=0.0060$) in evacuees and non-evacuees, respectively, after the disaster. Therefore, the subjects were classified into the normal HDL-C level group and hypo-HDL cholesterol group at baseline. Among men in the hypo-HDL cholesterol group (404 evacuees and 780 non-evacuees), the HDL-C levels significantly increased from 35.6±3.5 mg/dL to 37.8±6.7 mg/dL ($p<0.0001$) and 35.6±3.2 mg/dL to 38.4±6.1 mg/dL ($p<0.0001$) in evacuees and non-evacuees,

respectively. In addition, the ratio of smoking habit significantly decreased from 32.0% to 27.5% ($p<0.0001$) and 32.6% to 26.6% ($p<0.0001$) in evacuees and non-evacuees, respectively (Table 2). Although the change in the HDL-C levels did not differ significantly among evacuees and non-evacuees, increases in the BMI ($p<0.0001$), diastolic blood pressure ($p=0.019$), and AST level ($p=0.029$) were significantly greater in evacuees than non-evacuees (Table 3). Among the women (15,054 participants; 5,396 evacuees and 9,658 non-evacuees), the HDL-C levels significantly decreased from 62.3±14.2 mg/dL to 60.8±14.3 mg/dL ($p<0.0001$) in evacuees after the disaster, however, the HDL-C levels did not significantly change (61.9±14.2 mg/dL to 61.9±14.9 mg/dL; $p=0.7282$) in non-evacuees. The subjects were then classified into the normal HDL-C group and hypo-HDL cholesterol group at baseline. Among women in the

Table 2. continued

HDL-C ≥ 40mg/dL						
Men						
	Evacuees			Non-evacuees		
	Before	After	p value	Before	After	p value
Number	3,871			7,377		
Age (years)	66.6 ± 9.5	68.2 ± 9.5	< 0.0001	66.9 ± 9.3	68.3 ± 9.3	< 0.0001
Body weight (kg)	62.5 ± 9.7	64.3 ± 9.9	< 0.0001	61.8 ± 9.4	62.3 ± 9.6	< 0.0001
BMI (kg/m ²)	23.6 ± 3.1	24.4 ± 3.1	< 0.0001	23.4 ± 3.0	23.6 ± 3.0	< 0.0001
SBP (mmHg)	133.7 ± 17.4	134.8 ± 15.4	< 0.0001	132.5 ± 16.2	134.5 ± 16.0	< 0.0001
DBP (mmHg)	78.2 ± 10.3	79.9 ± 9.9	< 0.0001	78.5 ± 10.1	79.2 ± 10.2	< 0.0001
HbA1c (%)	5.55 ± 0.69	5.59 ± 0.79	< 0.0001	5.51 ± 0.66	5.52 ± 0.71	< 0.0001
HDL-C (mg/dL)	58.9 ± 13.5	55.9 ± 13.4	< 0.0001	58.0 ± 13.3	57.5 ± 13.8	< 0.0001
LDL-C (mg/dL)	115.6 ± 29.9	120.5 ± 31.1	< 0.0001	116.2 ± 29.1	116.7 ± 29.8	0.07
AST (IU/L)	27.2 ± 14.1	27.9 ± 12.0	0.003	26.3 ± 10.5	26.9 ± 12.7	< 0.0001
ALT (IU/L)	23.6 ± 16.1	26.5 ± 18.3	< 0.0001	22.4 ± 13.2	23.3 ± 15.3	< 0.0001
γ-GT (IU/L)	46.9 ± 64.1	49.8 ± 57.0	0.0003	44.5 ± 59.3	46.5± 67.9	0.0012
Smoking habit (%)						
Yes	24.6	21.4	< 0.0001	22.7	19.8	< 0.0001
No	75.4	78.6		77.3	80.2	
Drinking						
Everyday	48.8	46.9	< 0.0001	48.7	48.1	< 0.0001
Sometimes	22.7	21.1		22.3	21.8	
Little	13.4	14.7		14.0	14.9	
Never	15.1	17.3		15.0	15.1	
Women						
	Evacuees			Non-evacuees		
	Before	After	p value	Before	After	p value
Number	5,236			9,351		
Age (years)	65.9 ± 9.9	67.5 ± 9.9	< 0.0001	65.6 ± 9.1	67.1 ± 9.1	< 0.0001
Body weight (kg)	53.0 ± 8.6	53.8 ± 8.8	< 0.0001	52.3 ± 8.4	52.5 ± 8.6	< 0.0001
BMI (kg/m ²)	23.5 ± 3.5	24.0 ± 3.6	< 0.0001	23.2 ± 3.4	23.4 ± 3.5	< 0.0001
SBP (mmHg)	131.1 ± 17.7	131.8 ± 16.1	0.005	130.2 ± 16.8	132.5 ± 16.4	< 0.0001
DBP (mmHg)	75.4 ± 10.3	77.2 ± 9.9	< 0.0001	76.1 ± 10.1	77.2 ± 9.9	< 0.0001
HbA1c (%)	5.54 ± 0.64	5.51 ± 0.66	< 0.0001	5.48 ± 0.55	5.47 ± 0.57	0.004
HDL-C (mg/dL)	63.1 ± 13.7	61.4 ± 14.0	< 0.0001	62.8 ± 13.7	62.7 ± 13.9	< 0.0001
LDL-C (mg/dL)	124.1 ± 29.7	127.9 ± 32.1	< 0.0001	125.3 ± 29.2	125.5 ± 29.9	0.592
AST (IU/L)	23.9 ± 10.0	24.5 ± 10.6	< 0.0001	23.7 ± 8.2	23.9 ± 9.3	0.006
ALT (IU/L)	19.0 ± 12.5	20.5 ± 14.9	< 0.0001	18.5 ± 10.4	19.1 ± 11.9	< 0.0001
γ-GT (IU/L)	23.8 ± 31.3	25.6 ± 26.5	< 0.0001	23.5 ± 24.4	24.0 ± 22.7	0.009
Smoking habit (%)						
Yes	4.4	4.2	0.248	3.4	2.9	< 0.0001
No	95.6	95.8		96.6	97.1	
Drinking						
Everyday	5.7	5.9	< 0.0001	4.5	4.3	0.024
Sometimes	18.2	15.3		16.5	15.9	
Little	27.2	26.6		30.4	31.5	
Never	48.9	52.3		48.7	48.2	

Data are presented as mean $\pm$ S.D.BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, HbA1c: hemoglobin A1c, HDL-C: high density lipoprotein cholesterol, LDL-C: low density lipoprotein cholesterol, AST: aspartate aminotransferase, ALT: alanine aminotransferase, γ -GT: γ -glutamyl transpeptidase

hypo-HDL cholesterolemia group (160 evacuees and 307 non-evacuees), the HDL-C levels significantly increased from 36.3 $\pm$ 2.7 mg/dL to 40.1 $\pm$ 7.5 mg/dL (p <0.0001) and 36.1 $\pm$ 3.1 mg/dL to 39.5 $\pm$ 6.2 mg/dL (p <0.0001) in evacuees and non-evacuees, respectively, whereas the ratio of smoking habit did not significantly change in evacuees and non-evacuees. Additionally, the changes in the HDL-C levels and other risk factors did not differ significantly among evacuees and non-evacuees. On the other hand, among men in the normal HDL-C level group (3,871 evacuees and 7,377 non-evacuees), the HDL-C levels significantly decreased from 58.9 $\pm$ 13.5 mg/dL to 55.9 $\pm$ 13.4 mg/dL (p <0.0001) and 58.0 $\pm$ 13.3 mg/dL to 57.5 $\pm$ 13.8 mg/dL (p <0.0001) in evacuees and non-evacuees, respectively, whereas the ratio of smoking habit significantly decreased from 24.6% to 21.4% (p <

0.0001) and 22.7% to 19.8% (p <0.0001) in evacuees and non-evacuees, respectively (Table 2). Moreover, the decrease in the HDL-C levels was greater (p <0.0001) in evacuees than non-evacuees (Table 3), and increases in the BMI (p <0.0001), diastolic blood pressure (p =0.032), HbA1c (p =0.016), LDL-C (p <0.0001), and ALT levels (p <0.0001) were significantly greater in evacuees than non-evacuees. Among women in the normal HDL-C level group (5,236 evacuees and 9,351 non-evacuees), the HDL-C levels significantly increased from 63.1 $\pm$ 13.7 mg/dL to 61.4 $\pm$ 14.0 mg/dL (p <0.0001) and 62.8 $\pm$ 13.7 mg/dL to 62.7 $\pm$ 13.9 mg/dL (p <0.0001) in evacuees and non-evacuees, respectively. In addition, the ratio of smoking habit significantly decreased from 3.4% to 2.9% (p <0.0001) in only non-evacuees, respectively (Table 2). Additionally, a significantly greater decrease in

Table 3. Changes in Clinical and Biochemical Characteristics among Non-evacuees and Evacuees before and after the Great East Japan Earthquake.

	HDL-C<40mg/dL					
	Men			Women		
	Evacuees	Non-evacuees	p value	Evacuees	Non-evacuees	p value
Number	404	780		160	307	
Age (years)	1.6	1.4	0.002	1.7	1.4	0.000
Body weight (kg)	1.5	0.1	< 0.0001	0.2	-0.03	0.406
BMI (kg/m ²)	0.6	0.1	< 0.0001	0.2	0.0	0.148
SBP (mmHg)	3.1	1.4	0.078	-0.7	0.4	0.495
DBP (mmHg)	2.9	0.4	< 0.0001	1.8	0.3	0.154
HbA1c (%)	0.01	0.04	0.391	0.06	-0.02	0.063
HDL-C (mg/dL)	2.1	2.8	0.101	3.4	3.3	0.893
LDL-C (mg/dL)	6.5	3.6	0.081	7.7	6.4	0.648
AST (IU/L)	1.4	0.8	0.374	2.2	0.3	0.118
ALT (IU/L)	3.2	0.6	0.029	3.5	0.4	0.050
γ-GT (IU/L)	2.4	0.5	0.416	4.2	0.2	0.012

	HDL-C ≥ 40mg/dL					
	Men			Women		
	Evacuees	Non-evacuees	p value	Evacuees	Non-evacuees	p value
Number	3,871	7,377		5,236	9,351	
Age (years)	1.6	1.4	<.0001	1.6	1.5	< 0.0001
Body weight (kg)	1.8	0.5	<.0001	0.8	0.2	< 0.0001
BMI (kg/m ²)	0.8	0.2	<.0001	0.5	0.2	< 0.0001
SBP (mmHg)	1.1	1.9	0.013	0.7	2.2	< 0.0001
DBP (mmHg)	1.7	0.8	<.0001	1.8	1.0	<.0001
HbA1c (%)	0.04	0.02	0.016	-0.01	-0.03	0.019
HDL-C (mg/dL)	-3.0	-0.6	<.0001	-0.1	-1.7	< 0.0001
LDL-C (mg/dL)	4.9	0.5	<.0001	0.1	3.4	< 0.0001
AST (IU/L)	0.7	0.6	0.737	0.2	0.6	0.016
ALT (IU/L)	2.9	1.0	<.0001	0.6	1.6	< 0.0001
γ-GT (IU/L)	2.9	2.0	0.332	1.9	0.4	< 0.0001

Data are presented as mean ± S.D.

P value comparing the changes in the evacuee group to the changes in the non-evacuee group between before and after the earthquake.

BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, HbA1c: hemoglobin A1c, HDL-C: high density lipoprotein cholesterol, LDL-C: low density lipoprotein cholesterol, AST: aspartate aminotransferase, ALT: alanine aminotransferase, γ-GT: γ-glutamyl transpeptidase

Table 4. Multivariate Logistic Regression Analysis of Factors Influencing the Incidence of Hypo-HDL Cholesterolemia after the Great East Japan Earthquake.

Model	Total		Men		Women	
	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value
Evacuation	1.387 (1.214-1.584)	< 0.0001	1.413 (1.198-1.667)	< 0.0001	1.351 (1.078-1.693)	0.0089
Age (years)	1.019 (1.011-1.026)	< 0.0001	1.017 (1.008-1.027)	0.0004	1.021 (1.008-1.035)	0.0018
Sex (0, men; 1, women)	0.376 (0.323-0.437)	< 0.0001				
BMI (kg/m ²)	1.106 (1.084-1.129)	< 0.0001	1.129 (1.099-1.159)	< 0.0001	1.074 (1.040-1.109)	< 0.0001
Change in BMI (1 kg/m ²)	1.205 (1.141-1.272)	< 0.0001	1.197 (1.116-1.285)	< 0.0001	1.222 (1.121-1.332)	< 0.0001
Daily drinking (0, no; 1, yes)	0.709 (0.517-0.972)	0.0326	0.714 (0.518-0.986)	0.0406	1.129 (0.148-8.623)	0.9068
Current smoking (0, no; 1, yes)	1.574 (1.318-1.880)	< 0.0001	1.618 (1.339-1.954)	< 0.0001	1.354 (0.758-2.417)	0.3056
SBP (mmHg)	1.001 (0.997-1.005)	0.5995	1.002 (0.997-1.007)	0.5242	1.000 (0.993-1.007)	0.9624
ALT (IU/L)	1.384 (1.166-1.643)	0.0002	1.238 (1.004-1.527)	0.0456	1.657 (1.224-2.243)	0.0011
γ-GT (IU/L)	0.791 (0.695-0.900)	0.0004	0.766 (0.660-0.890)	0.0005	0.871 (0.672-1.129)	0.2971
Diabetes	1.284 (1.048-1.573)	0.0157	1.237 (0.973-1.573)	0.0827	1.365 (0.932-1.999)	0.1097

Data are presented as odds ratio (95% confidence interval).

OR: odds ratio, CI: confidence interval, BMI: body mass index, SBP: systolic blood pressure, ALT: alanine aminotransferase, γ-GT: γ-glutamyl transpeptidase

Diabetes was defined as a fasting plasma glucose level ≥126 mg/dL (7.0 mmol/L), HbA1c level ≥6.5%, or self-reported use of antihyperglycemic drugs.

the HDL-C level ($p<0.0001$) was observed in evacuees compared with non-evacuees (Table 3), and increases in the BMI ($p<0.0001$), diastolic blood pressure ($p=0.006$), LDL-C ($p<0.0001$), AST ($p=0.016$), ALT ($p<0.0001$), and γ-GT levels ($p<0.0001$) were significantly greater in evacuees than non-evacuees.

Risk factors for the incidence of hypo-HDL-cholesterolemia after disaster

A multivariate logistic regression analysis was performed to identify independent associations among baseline risk factors and the incidence of hypo-HDL cholesterolemia after

Table 5. Incidence of Hypo-HDL Cholesterolmia Following the Great East Japan Earthquake.

HDL-C $\geq$ 40 mg/dL before the Earthquake	Incidence of hypo-HDL cholesterolmia (< 40 mg/dL) after the Earthquake (n)			
	Total	Non-evacuees	Evacuees	p value*
Total (n = 25,835)	3.81% (985)	3.23% (540)	4.89% (445)	< 0.0001
Men (n = 11,248)	5.88% (661)	4.93% (364)	7.67% (297)	< 0.0001
Women (n = 14,587)	2.22% (324)	1.88% (176)	2.83% (148)	0.0002

Data are presented as percentage (number).

*p value comparing the incidence of hypo-HDL cholesterolmia after the Earthquake between the evacuee group and the non-evacuee group.

the disaster (Table 4). The evacuation was significantly associated with the incidence of hypo-HDL cholesterolmia [odds ratio (OR) 1.387, $p < 0.0001$] after adjusting for age, sex, BMI, smoking status, systolic blood pressure, diabetes, and ALT and γ -GT levels. The baseline BMI, an increase of BMI (1 kg/m^2), daily drinking, current smoking, ALT and γ -GT levels, and diabetes were also significantly associated with the incidence of hypo-HDL cholesterolmia (OR 1.106, $p < 0.0001$; OR 1.205, $p < 0.0001$; OR 0.709, $p = 0.00326$; OR 1.574, $p < 0.0001$; OR 1.384, $p = 0.0002$ and OR 0.791, $p = 0.0004$; and OR 1.284, $p = 0.0157$, respectively). In the gender-segregated multivariate logistic regression analysis, the evacuation was significantly associated with the incidence of hypo-HDL-cholesterolmia in both men (OR 1.413, $p < 0.0001$) and women (OR 1.351, $p = 0.0089$) after adjusting for age, BMI, smoking status, systolic blood pressure, diabetes, and ALT and γ -GT levels. The baseline BMI, an increase of BMI (1 kg/m^2), and ALT were also significantly associated with the incidence of hypo-HDL cholesterolmia in both men (OR 1.129, $p < 0.0001$; OR 1.197, $p < 0.0001$; and OR 1.238, $p = 0.0456$, respectively) and women (OR 1.074, $p < 0.0001$; OR 1.222, $p < 0.0001$; and OR 1.657, $p = 0.0011$, respectively). Additionally, daily drinking, current smoking, and γ -GT were also significantly associated with the incidence of hypo-HDL cholesterolmia in men (OR 0.714, $p = 0.0406$; OR 1.618, $p < 0.0001$; and OR 0.766, $p = 0.0005$, respectively).

Incidence of hypo-HDL cholesterolmia after the disaster

The crude incidence of hypo-HDL cholesterolmia in the normal HDL-C level group (25,835 subjects) was 3.81% (985 subjects). Furthermore, the crude incidence of hypo-HDL cholesterolmia was 5.88% (661 subjects) in men (11,248 subjects) and 2.22% (324 subjects) in women (14,587 subjects; Table 4). Specifically, in the normal HDL-C level group (9,107 evacuees and 16,728 non-evacuees), the crude incidence of hypo-HDL cholesterolmia was significantly higher ($p < 0.0001$; Table 5) in evacuees (4.89%; 445 subjects) than non-evacuees (3.23%; 540 subjects). In addition, in men (3,871 evacuees and 7,377 non-evacuees), the crude incidence of hypo-HDL cholesterolmia was significantly higher ($p < 0.0001$; Table 4) in evacuees (7.67%; 297 subjects) than non-evacuees (4.93%; 364 subjects). In women (5,236 evacuees and 9,351 non-evacuees), the inci-

dence of hypo-HDL cholesterolmia was also significantly higher ($p = 0.0002$; Table 5) in evacuees (2.83%; 148 subjects) than non-evacuees (1.88%; 176 subjects).

Discussion

The present study demonstrated that the prevalence of hypo-HDL cholesterolmia was significantly increased in evacuees compared to non-evacuees after the Great East Japan Earthquake and Fukushima Daiichi nuclear disaster. All metabolic factors including the BMI, blood pressure, glucose metabolism, lipid metabolism, and liver function were adversely affected in the normal HDL-C level group. In addition, the decrease in HDL-C was significantly greater in evacuees than non-evacuees in the normal HDL-C level group. Moreover, adverse effects on all metabolic factors, including the BMI, blood pressure, glucose metabolism, lipid metabolism, and liver function, were significantly more prevalent in male evacuees in the normal HDL-level group compared to non-evacuees. On the other hand, in the hypo-HDL cholesterolmia group, the levels of HDL-C significantly increased after the disaster, however, the other metabolic factors, except glucose metabolism, were significantly and negatively affected. Furthermore, the present study also showed that the evacuation was significantly associated with the incidence of hypo-HDL cholesterolmia and the incidence of hypo-HDL cholesterolmia was significantly higher in evacuees than non-evacuees. Thus, this historic disaster was more likely to have a negative effect on metabolic laboratory test results in the evacuees group than the non-evacuees group. These findings suggest that chronic metabolic health problems such as obesity, type 2 diabetes, hypertension and dyslipidemia should be carefully monitored and treated after the disaster, especially in evacuees.

Substantial epidemiological studies have demonstrated that the HDL-C level is a strong, independent, and inverse risk factor of CVD (15, 16) and CVA (5, 6). Hypo-HDL cholesterolmia is strongly and inversely associated with the risk for coronary heart disease (17) and cerebrovascular disease (18). The high HDL-C level exerts its cardio-protective effect primarily through its role in reverse cholesterol transport and its anti-inflammatory, anti-thrombotic and antioxidative properties. As endogenous estrogens have a favorable effect on lipid metabolism, women often have higher HDL-C levels than men (19). Additionally, alcohol consumption

can increase the HDL-C levels. Various metabolic and environmental factors, including acute or chronic infection, a high intake of refined carbohydrates and cigarette smoking, can decrease the HDL-C levels. Importantly, a low HDL-C level is likely a secondary effect from components of metabolic syndrome: insulin resistance, obesity, high triglyceride dyslipidemia, and chronic low grade inflammation (20). A life as an evacuee in unfavorable conditions increases stress in terms of privacy, food availability, duty assignments, financial stability and health (21). Natural disasters have been shown to have a negative impact on metabolic factors (22). After the Great Hanshin-Awaji Earthquake, glycemic control was aggravated in diabetic patients, and an association among chronic life-threatening stress and a worsening of metabolic control has been suggested (21). Similar effects have been reported with hypertension, with ambulatory blood pressure revealing that sympathetic activation is an important component of rising blood pressure after life-threatening events and may trigger myocardial infarction (23).

Our data showed that the negative effects on metabolic factors were greater in evacuees than non-evacuees. These differences might be related to changes in lifestyle such as diet, physical activity, and life environment before and after the evacuation. It has been demonstrated that the change of lifestyle is strongly associated with the prevalence of hypo-HDL cholesterolemia. However, our results were obtained from a follow-up period of only 1.6 years. Therefore, it is necessary to evaluate these effects by a further long-term follow-up.

In conclusion, this is the first report to reveal that the evacuation was associated with the risk of incidence of hypo-HDL cholesterolemia, leading to an increase in CVD. This information could be very important for periodic health checkups and lifestyle recommendations for evacuees in the future.

The findings and conclusions of this article are solely the responsibility of the authors and do not represent the official views of the Fukushima Prefectural Government.

The authors state that they have no Conflict of Interest (COI).

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