

**Fig. 1.** (A) Location of the Miyagi prefecture and the epicenter of the Great East Japan Earthquake (black cross) and the largest aftershock (gray cross). The municipalities in the Miyagi Prefecture facing the Pacific Ocean were defined as the seacoast area (shown in red) and the other area as the inland area (shown in blue). (B) The weekly occurrence of cardiopulmonary arrest of presumed cardiac origin. \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$  vs. 2008–2010.

occurrence of CPA. Additionally, since our Miyagi Prefecture was damaged most seriously among those prefectures [1,2], the discrepancy might be attributable to the severity of physical and emotional stress.

Moreover, the present study demonstrated that time-dependent changes of the incidence of CPA after the Earthquake were influenced by several factors including age, sex, and residence, and their influences could dramatically vary depending on the phases after the Earthquake and the occurrence of aftershocks. As previously reported, the elderly is a high risk group for cardiovascular events caused by increases in sympathetic nervous activity, coagulation activity and comorbidity such as hypertension after earthquakes [4]. The present results indicate that the elderly should be treated more carefully over the long term after a disaster, especially with aftershock occurrences, to prevent sudden death. Since the general population in developed countries including Japan has been rapidly growing older [9], it will take on added significance on how to treat the elderly people over the long term after the earthquake disaster.

Two limitations should be mentioned for this study. First, it is possible that the number of CPA patients was underestimated, especially in the seacoast areas with severe damages. Second, since this study was observationally-designed, the precise mechanisms of the increase in CPA after the Earthquake remain to be elucidated.

In conclusion, the present study indicated that the increase in the occurrence of CPA after the Earthquake was influenced by sex, age, and residence, and that their influences could change depending on the phases after the Earthquake and the occurrence of aftershock. We consider that the present study may provide a clue to reduce the occurrence of CPA in future disasters.

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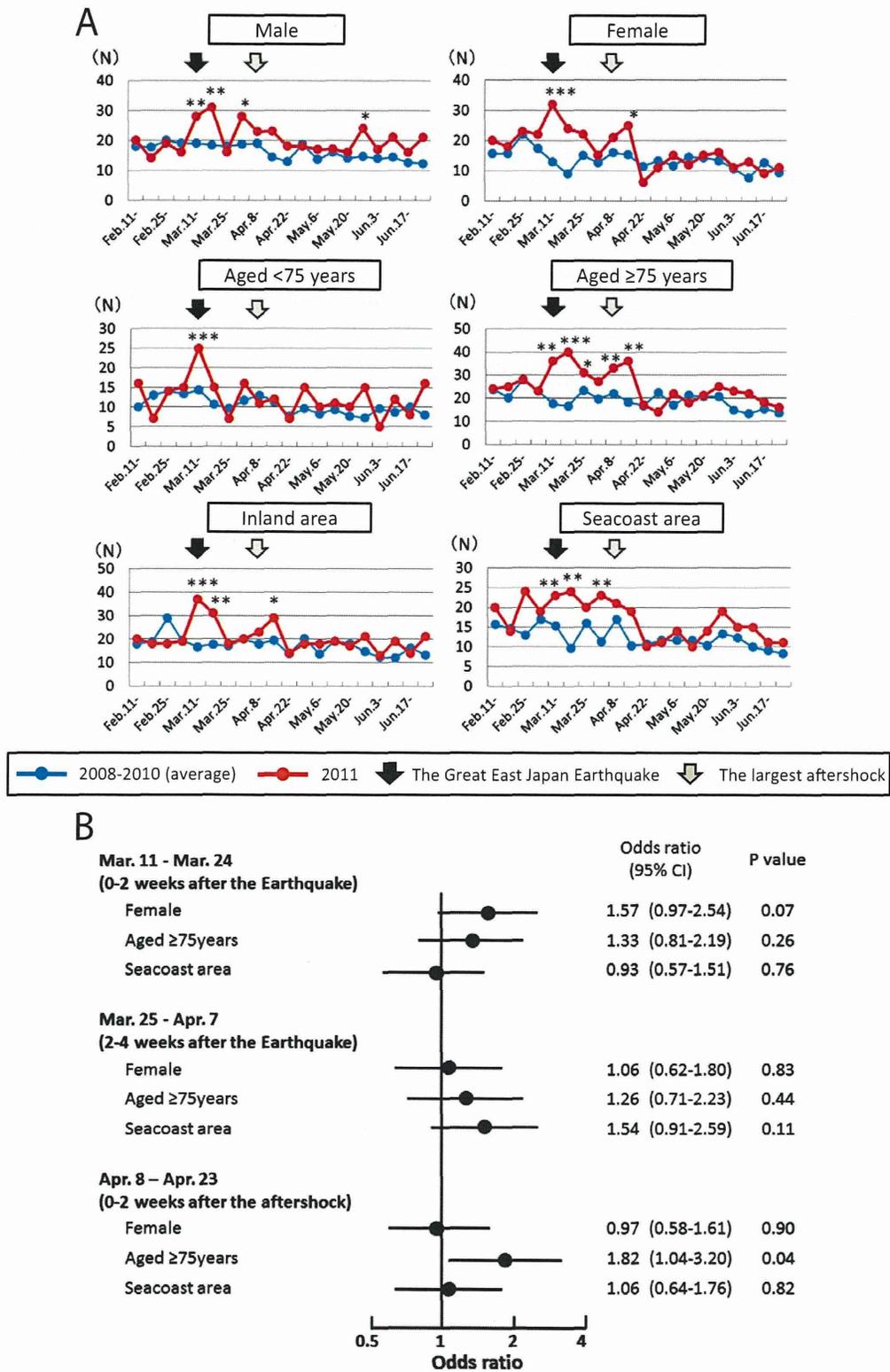
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**Disclosure statement**

The authors have nothing to disclose.

**Conflict of interest**

The authors report no relationships that could be construed as a conflict of interest.



**Fig. 2.** (A) Sub-group analysis regarding gender, sex (<75 or ≥75 years), and residence (seacoast or inland area). \*P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001 vs. 2008–2010. (B) Multivariate logistic regression to identify the factors that contributed to the increase in CPA during the following 3 periods after the Earthquake; March 11–24 (0–2 weeks after the Earthquake), March 25–April 7 (2–4 weeks after the Earthquake), and April 8–23 (0–2 weeks after the largest aftershock).

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## References

- [1] Japan Meteorological Agency. Information on the 2011 off the Pacific Coast of Tohoku earthquake. [http://www.jma.go.jp/jma/en/2011\\_Earthquake/information\\_on\\_2011\\_Earthquake.html](http://www.jma.go.jp/jma/en/2011_Earthquake/information_on_2011_Earthquake.html). [Accessed August 12, 2014].
- [2] National Police Agency of Japan. Damage situation and police countermeasures associated with 2011 Tohoku district – off the Pacific Ocean earthquake. [https://www.npa.go.jp/archive/keibi/biki/higaijokyo\\_e.pdf](https://www.npa.go.jp/archive/keibi/biki/higaijokyo_e.pdf). [Accessed August 12, 2014].
- [3] Leor J, Poole WK, Kloner RA. Sudden cardiac death triggered by an earthquake. *N Engl J Med* 1996;334:413–9.
- [4] Kario K, McEwen BS, Pickering TG. Disasters and the heart: a review of the effects of earthquake-induced stress on cardiovascular disease. *Hypertens Res* 2003;26:355–67.
- [5] Schwartz BG, French WJ, Mayeda GS, et al. Emotional stressors trigger cardiovascular events. *Int J Clin Pract* 2012;66:631–9.
- [6] Aoki T, Fukumoto Y, Yasuda S, et al. The Great East Japan Earthquake disaster and cardiovascular diseases. *Eur Heart J* 2012;33:2796–803.
- [7] Kitamura T, Kiyohara K, Iwami T. The Great East Japan Earthquake and out-of-hospital cardiac arrest. *N Engl J Med* 2013;369:2165–7.
- [8] Niiyama M, Tanaka F, Nakajima S, et al. Population-based incidence of sudden cardiac and unexpected death before and after the 2011 earthquake and tsunami in Iwate, northeast Japan. *J Am Heart Assoc* 2014;3:e000798. <http://dx.doi.org/10.1161/JAHA.114.000798>.
- [9] Statistics Bureau, Ministry of Internal Affairs and Communications, Japan. About 2010 Population Census of Japan. [http://www.stat.go.jp/english/data/kokusei/2010/final\\_en/pdf/summary.pdf](http://www.stat.go.jp/english/data/kokusei/2010/final_en/pdf/summary.pdf). [Accessed August 12, 2014].



## Predictors and Prognostic Impact of Post-Traumatic Stress Disorder After the Great East Japan Earthquake in Patients With Cardiovascular Disease

– Report From the CHART-2 Study –

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Hiroaki Shimokawa, MD, PhD on behalf of the CHART-2 Investigators

**Background:** We examined the prevalence, predictors and prognostic impact of post-traumatic stress disorder (PTSD) after the Great East Japan Earthquake in patients with cardiovascular disease (CVD) in the CHART-2 study.

**Methods and Results:** The prevalence of PTSD was 14.7% at 6 months after the Earthquake. Female sex, experiencing the Tsunami, property loss, poverty, and insomnia medication use were associated with PTSD. The patients with PTSD more frequently experienced a composite of death, acute myocardial infarction, stroke and heart failure (18.5% vs. 15.0%,  $P=0.035$ ).

**Conclusions:** PTSD was frequent in CVD patients after the Earthquake and had an adverse prognostic impact. (*Circ J* 2011; ■■: ■■■■–■■■■)

**Key Words:** Cardiovascular disease; Great East Japan Earthquake; Post-traumatic stress disorder

In March 2011, the Great East Japan Earthquake, followed by a devastating tsunami and Fukushima-Daiichi nuclear power plant explosion, destroyed 370,780 houses and killed 15,785 people in the Tohoku District of Japan.<sup>1–3</sup> Our observational study, the Chronic Heart Failure Analysis and Registry in the Tohoku District-2 (CHART-2),<sup>4,6</sup> which enrolled 10,219 patients with cardiovascular disease (CVD) in the disaster area, has provided a unique opportunity to examine the prognostic impact of disaster-related mental stress in survivors with CVD.

### Methods

The CHART-2 study is a multicenter observational study of Japanese patients with CVD (Identifier: NCT00418041).<sup>4–6</sup> Briefly, the study enrolled 10,219 consecutive Japanese patients older than 20 years with heart failure (HF) in Stages B/C/D or those with coronary artery disease (Stage A) between October 2006 and March 2010. Stages of HF were defined according to the ACC/AHA guidelines.<sup>7</sup> Information on medical history and baseline demographics, including medication and

echocardiographic data, was collected at the time of enrollment and thereafter annually by clinical research coordinators. The CHART-2 study was approved by the local ethics committees and written informed consent was provided by all patients. In September 2011, we sent a self-administered questionnaire including the Japanese version of the Impact of Event Scale-Revised (IES-R-J, Cronbach's Alpha; 0.95)<sup>8</sup> to 8,823 patients registered in the CHART-2 study. The IES-R-J score ranges from 0 to 88, and post-traumatic stress disorder (PTSD) is defined as a score  $\geq 25$ .<sup>8</sup> The primary endpoint was a composite of all-cause mortality and hospitalization for acute myocardial infarction, angina pectoris, stroke and HF. The present study was approved by the ethics committee of each participating hospital. All analyses were performed using R version 3.0.3 (R Foundation for Statistical Computing, Vienna, Austria).

### Results

By December 2011, we obtained 3,620 valid responses, among which 534 (14.7%) patients were diagnosed as having PTSD.

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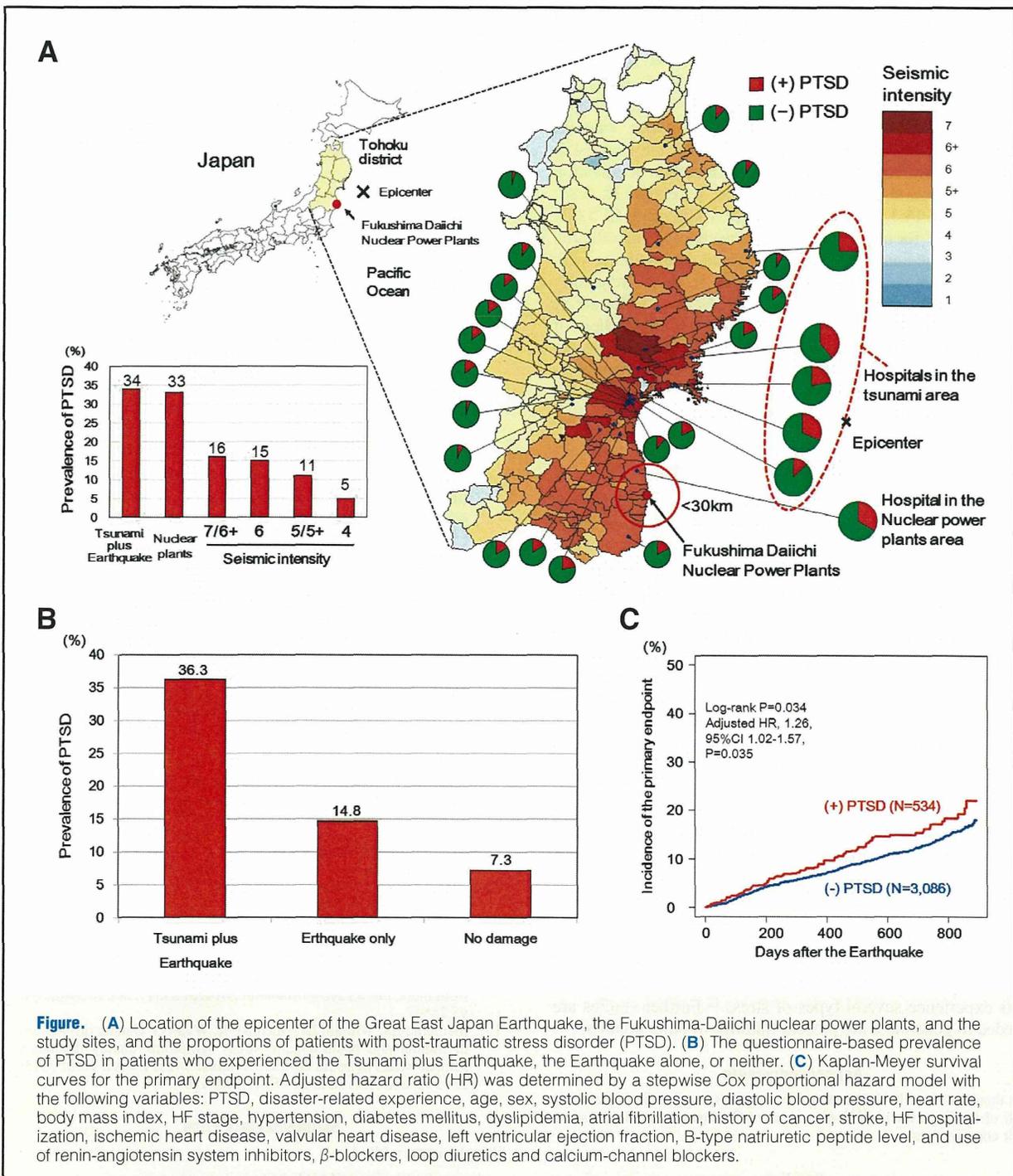
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Table. Baseline Characteristics of the Patients	PTSD		P value
	Yes (n=534)	No (n=3,086)	
Age at questionnaire, mean (SD), years	68.2 (10.9)	66.6 (11.4)	0.002
Female sex, n (%)	205 (38.4)	756 (24.5)	<0.001
Height, mean (SD), cm	159.2 (8.9)	161.5 (8.9)	<0.001
Body weight, mean (SD), kg	61.4 (12.3)	63.2 (11.6)	0.002
Body mass index, mean (SD), kg/m <sup>2</sup>	24.1 (4.2)	23.9 (4.2)	0.417
SBP, mean (SD), mmHg	127.5 (18.2)	128.1 (17.1)	0.504
DBP, mean (SD), mmHg	72.8 (11.5)	74.2 (11.5)	0.01
Heart rate, mean (SD), beats/min	69.5 (13.5)	70.2 (13.7)	0.253
Current or past smoking, n (%)	222 (44.6)	1,446 (49.4)	0.047
<b>Echocardiography and laboratory findings</b>			
LVEF, mean (SD), %	62.2 (14.1)	62.0 (13.8)	0.84
LVEF <50%	100 (20.0)	560 (19.1)	0.624
Left atrial dimension, mean (SD), mm	40.3 (8.4)	40.4 (7.8)	0.86
Hemoglobin, mean (SD), g/dl	13.4 (2.1)	13.7 (1.8)	<0.001
Total protein, mean (SD), g/dl	7.3 (2.8)	7.2 (0.6)	0.305
Albumin, mean (SD), g/dl	4.2 (0.4)	4.2 (0.4)	0.348
Total cholesterol, mean (SD), mg/dl	184.8 (35.5)	184.7 (34.8)	0.963
HbA1c, mean (SD), %	5.8 (11.5)	5.9 (2.5)	0.712
eGFR, mean (SD), ml·min <sup>-1</sup> ·1.73m <sup>-2</sup>	64.6 (28.3)	65.8 (22.8)	0.383
BNP, median (25th, 75th percentiles), pg/ml	59.2 (24.5, 129.6)	50.4 (21.6, 119.8)	0.025
<b>Medical history, n (%)</b>			
Heart failure in Stage C/D	234 (43.8)	1,272 (41.2)	0.274
Hypertension	394 (73.8)	2,348 (76.1)	0.251
Diabetes mellitus	127 (23.8)	756 (24.5)	0.744
Dyslipidemia	385 (72.1)	2,386 (77.3)	0.009
Hemodialysis	5 (0.9)	23 (0.7)	0.594
Stroke	94 (17.6)	434 (14.1)	0.039
Atrial fibrillation	138 (26.0)	716 (23.3)	0.184
Cancer	49 (9.2)	313 (10.1)	0.601
COPD	9 (4.6)	35 (2.8)	0.175
Ischemic heart disease	272 (50.9)	1,764 (57.2)	0.008
Valvular heart disease	96 (18.0)	502 (16.3)	0.344
Cardiomyopathy	67 (12.5)	422 (13.7)	0.537
<b>Medications, n (%)</b>			
ACEI or ARB	335 (62.7)	1,967 (63.7)	0.661
Loop diuretics	133 (24.9)	632 (20.5)	0.025
Aldosterone antagonists	67 (12.5)	346 (11.2)	0.376
Calcium-channel blockers	242 (45.3)	1,422 (46.1)	0.778
Digitalis	72 (13.5)	407 (13.2)	0.836
β-blockers	209 (39.1)	1,293 (41.9)	0.235
Past or current insomnia medication use	194 (36.3)	171 (5.5)	<0.001
<b>Disaster experience, n (%)</b>			
No effect from the Earthquake	60 (11.2)	733 (23.8)	<0.001
Tsunami evacuation or being trapped	82 (15.4)	144 (4.7)	<0.001
Own hospitalization	43 (8.1)	65 (2.1)	<0.001
Hospitalization of close relatives	102 (19.1)	223 (7.2)	<0.001
Major property loss	238 (44.6)	857 (27.8)	<0.001
Economic poverty	69 (12.9)	96 (3.1)	<0.001
Change of residence	58 (10.9)	102 (3.3)	<0.001
Unemployment or job change	22 (4.1)	43 (1.4)	<0.001

Comparisons between groups were performed by the Welch's t-test for continuous variables, and by the Fisher's exact test for dichotomous variables. All analyses were performed using R version 3.0.3. P<0.05 was considered to be statistically significant. ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; BNP, B-type natriuretic peptide; COPD, chronic obstructive pulmonary disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HbA1c, hemoglobin A1c; LVEF, left ventricular ejection fraction; SBP, systolic blood pressure.



**Figure.** (A) Location of the epicenter of the Great East Japan Earthquake, the Fukushima-Daiichi nuclear power plants, and the study sites, and the proportions of patients with post-traumatic stress disorder (PTSD). (B) The questionnaire-based prevalence of PTSD in patients who experienced the Tsunami plus Earthquake, the Earthquake alone, or neither. (C) Kaplan-Meier survival curves for the primary endpoint. Adjusted hazard ratio (HR) was determined by a stepwise Cox proportional hazard model with the following variables: PTSD, disaster-related experience, age, sex, systolic blood pressure, diastolic blood pressure, heart rate, body mass index, HF stage, hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, history of cancer, stroke, HF hospitalization, ischemic heart disease, valvular heart disease, left ventricular ejection fraction, B-type natriuretic peptide level, and use of renin-angiotensin system inhibitors,  $\beta$ -blockers, loop diuretics and calcium-channel blockers.

The patients with PTSD were characterized by female sex, higher age, lower diastolic blood pressure, lower prevalence of ischemic heart disease, higher prevalence of stroke and, particularly, a higher frequency of a past or current history of insomnia medication use (Table). The prevalence of PTSD was highest in the hospitals in the area directly affected by the Tsunami or within close proximity (<30km) to the Fukushima-Daiichi nuclear power plant, and decreased in association with the reduction in seismic intensity (Figure A). The patients

who experienced the Tsunami had the highest prevalence of PTSD (Figure B). Multivariate logistic regression analysis revealed that PTSD was significantly associated with several factors, including female sex (adjusted odds ratio (adOR) 1.27; 95% confidence interval (CI) 1.02–1.57;  $P=0.02$ ), dyslipidemia (adOR 0.58; 95% CI 0.38–0.93;  $P=0.02$ ), past or current insomnia medication use (adOR 8.57; 95% CI 5.76–12.76;  $P<0.001$ ), experiencing the Tsunami (adOR 1.95; 95% CI 1.00–3.67;  $P=0.04$ ), major property loss (adOR 1.65; 95% CI

1.14–2.38;  $P < 0.01$ ) and economic poverty after the Earthquake (adOR 3.22; 95% CI 1.73–5.91;  $P < 0.001$ ). Interestingly, dyslipidemia (adOR 0.52; 95% CI 0.31–0.92;  $P = 0.02$ ), major property loss (adOR 1.78; 95% CI 1.15–2.72;  $P < 0.01$ ) and economic poverty (adOR 4.64; 95% CI 2.33–9.12;  $P < 0.001$ ) were more likely associated with PTSD in males, whereas experiencing the Tsunami (adOR 4.40; 95% CI 1.26–14.7;  $P = 0.02$ ) was in females. Past or current insomnia medication use had comparable effect between the sexes (adOR 8.80; 95% CI 5.30–14.1;  $P < 0.001$ , and adOR 10.00; 95% CI 5.00–20.4;  $P < 0.001$  for male and female, respectively). Importantly, during the median follow-up of 2 years, the patients with PTSD, as compared with those without it, more frequently experienced the primary endpoint (18.5% vs. 15.0%, adOR 1.26; 95% CI 1.02–1.57,  $P = 0.035$ ) (Figure C), regardless of age, sex, HF etiology or stage. Corporeal damages by the Tsunami and/or by the Earthquake did not influence the incidence of the primary endpoint (adOR 0.99; 95% CI 0.80–1.23,  $P = 0.93$ ) regardless of the presence or absence of PTSD.

## Discussion

To the best of our knowledge, this is the first study demonstrating the prevalence, predictors and adverse prognostic impact of psychological stress caused by a major earthquake. Although the overall prevalence of PTSD (11.4%) was comparable with that reported in the general population after major disasters,<sup>9,10</sup> the present study demonstrates for the first time that the intensity of the Earthquake, experiencing the Tsunami and proximity to the nuclear power plants were independently associated with the incidence of PTSD. PTSD was more frequently observed in females than in males,<sup>11</sup> and furthermore, sex differences were suggested in the mechanisms of PTSD after the Earthquake; dyslipidemia, major property loss and economic poverty were mainly associated with PTSD in males, whereas the Tsunami experience was the main factor for females. Thus, corporeal and spiritual losses differently influence mental disorders in males and females after a major natural disaster. In contrast, the prognostic effect of the Earthquake was comparable between the sexes in patients with PTSD.

In conclusion, PTSD was frequently noted in CVD patients at 6 months after the Great East Japan Earthquake and associated with subsequent adverse prognostic impact. Furthermore, the present study demonstrates the importance of a sex-based approach to preventing PTSD after major disasters when victims experience several types of stress.<sup>12</sup> Further studies are needed to generalize the present findings to other cohorts.

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## Conflict of Interest

H.S. received lecture fees from Bayer Yakuhin, Ltd (Osaka, Japan),

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## References

- Aoki T, Fukumoto Y, Yasuda S, Sakata Y, Ito K, Takahashi J, et al. The Great East Japan Earthquake Disaster and cardiovascular diseases. *Eur Heart J* 2012; **33**: 2796–2803.
- Shigemura J, Tanigawa T, Saito I, Nomura S. Psychological distress in workers at the Fukushima nuclear power plants. *JAMA* 2012; **308**: 667–669.
- Nakano M, Kondo M, Wakayama Y, Kawana A, Hasebe Y, Shafee MA, et al. Increased incidence of tachyarrhythmias and heart failure hospitalization in patients with implanted cardiac devices after the Great East Japan Earthquake Disaster. *Circ J* 2012; **76**: 1283–1285.
- Shiba N, Nochioka K, Miura M, Kohno H, Shimokawa H; CHART-2 Investigators. Trend of westernization of etiology and clinical characteristics of heart failure patients in Japan: First report from the CHART-2 study. *Circ J* 2011; **75**: 823–833.
- Nochioka K, Sakata Y, Fukumoto Y, Shiba N, Shimokawa H; CHART-2 Investigators. Prognostic impact of nutritional status in asymptomatic patients with cardiac diseases: A report from the CHART-2 Study. *Circ J* 2013; **77**: 2318–2326.
- Sakata Y, Miyata S, Nochioka K, Miura M, Shimokawa H. Gender differences in clinical characteristics, treatment and long-term outcome in patients with stage C/D heart failure in Japan: Report from the CHART-2 study. *Circ J* 2014; **78**: 2276–2283.
- Writing Committee Members: Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Drazner MH, et al. American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of heart failure: A report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation* 2013; **128**: e240–e327, doi:10.1161/CIR.0b013e31829e8776.
- Asukai N, Kato H, Kawamura N, Kim Y, Yamamoto J, Miyake Y, et al. Reliability and validity of the Japanese-language version of the impact of event scale-revised (IES-R-J): Four studies of different traumatic events. *J Nerv Ment Dis* 2002; **190**: 175–182.
- Norris FH, Friedman MJ, Watson PJ, Byrne CM, Diaz E, Kaniasty K. 60,000 disaster victims speak. Part I: An empirical review of the empirical literature, 1981–2001. *Psychiatry* 2002; **65**: 207–239.
- Goenjian AK, Steinberg AM, Najarian LM, Fairbanks LA, Tashjian M, Pynoos RS. Prospective study of posttraumatic stress, anxiety, and depressive reactions after earthquake and political violence. *Am J Psychiatry* 2000; **157**: 911–916.
- Charak R, Armour C, Elklit A, Angmo D, Elhai JD, Koot HM. Factor structure of PTSD, and relation with gender in trauma survivors from India. *Eur J Psychotraumatol* 2014; **5**: 25547, doi:10.3402/ejpt.v5.25547.
- Idemudia ES, William JK, Boehnke K, Wyatt G. Gender differences in trauma and posttraumatic stress symptoms among displaced Zimbabweans in South Africa. *J Trauma Stress Disord Treat* 2013; **2**: 1340, doi:10.4172/2324–8947.1000110.

## Supplementary Files

### Supplementary File 1

#### Appendix S1. The CHART-2 Study Investigators

Please find supplementary file(s);  
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