Circulation Journal
Official Journal of the Japanese Circulation Society
http://www.j-circ.or.jp

RAPID COMMUNICATION

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 –

Takeo Onose, MD; Kotaro Nochioka, MD, PhD; Yasuhiko Sakata, MD, PhD; Masanobu Miura, MD, PhD; Soichiro Tadaki, MD; Ryoichi Ushigome, MD; Takeshi Yamauchi, MD; Kenjiro Sato, MD; Kanako Tsuji, MD; Ruri Abe, MD; Satoshi Miyata, PhD; Jun Takahashi, MD, PhD; 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* 2015; **79:** 664–667)

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.[1–3] Our observational study, the Chronic Heart Failure Analysis and Registry in the Tohoku District-2 (CHART-2),[4–6] 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).[4–6] 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.[7] 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)[8] 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 ≥25.[8] 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.

Received December 24, 2014; revised manuscript received February 1, 2015; accepted February 2, 2015; released online February 13, 2015 Time for primary review: 13 days

Departments of Cardiovascular Medicine and Evidence-based Cardiovascular Medicine, Tohoku University Graduate School of Medicine, Sendai, Japan

The Guest Editor for this article was Hiroshi Ito, MD.

Mailing address: Yasuhiko Sakata, MD, PhD, Department of Cardiovascular Medicine, Tohoku University Graduate School of Medicine, 1-1 Seiryo-machi, Aoba-ku, Sendai 980-8574, Japan. E-mail: sakatayk@cardio.med.tohoku.ac.jp

ISSN-1346-9843 doi:10.1253/circj.CJ-14-1403

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/m²	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
Echocardiography and laboratory findings			
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), $ml \cdot min^{-1} \cdot 1.73 m^{-2}$	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
Medical history, n (%)			
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
Medications, n (%)			
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
Disaster experience, n (%)			
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.

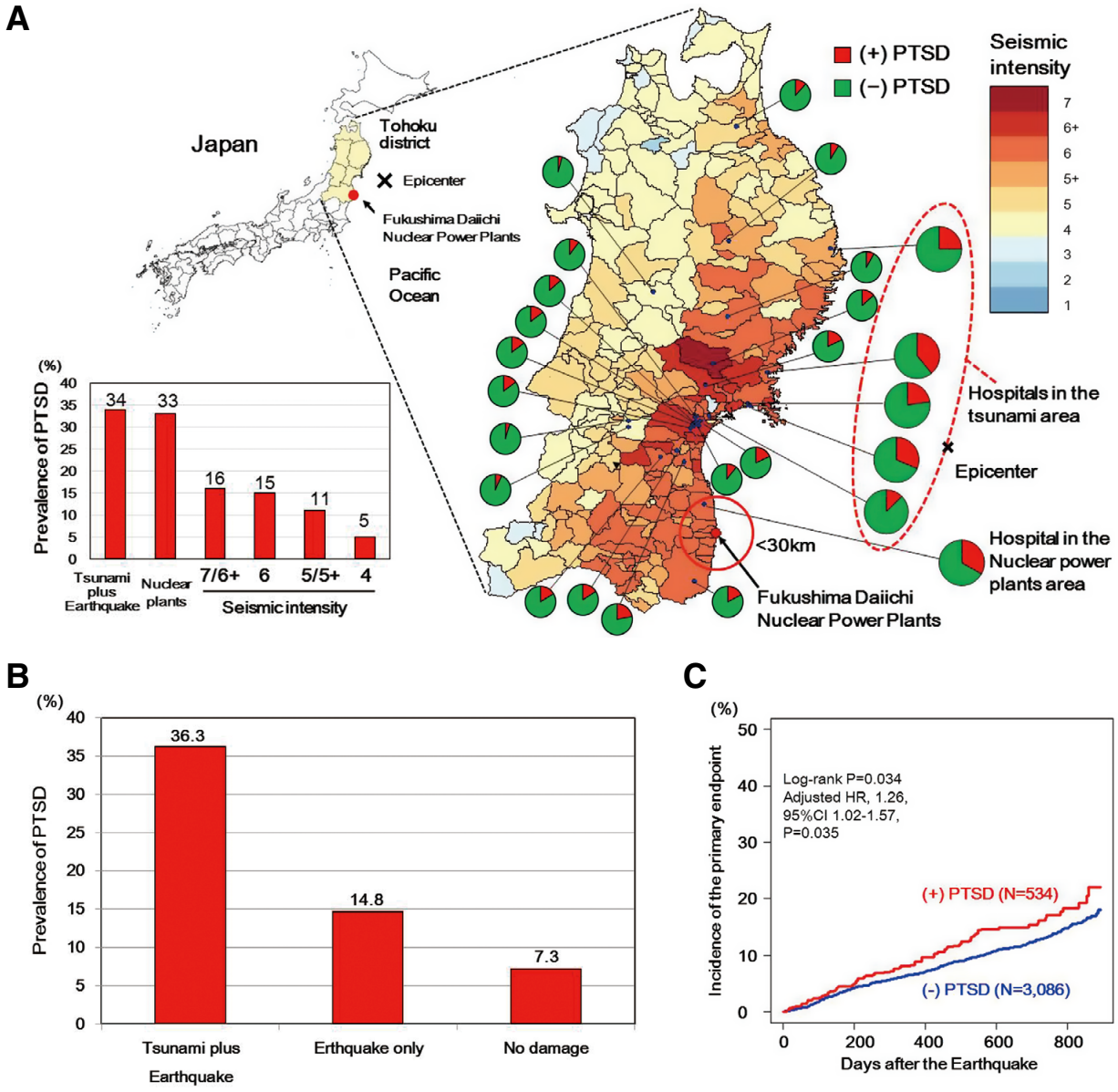

Figure. (**A**) Location of the epicenter of the Great East Japan Earthquake, the Fukushima-Daiichi nuclear power plants, and the study sites, and the proportions of patients with post-traumatic stress disorder (PTSD). (**B**) The questionnaire-based prevalence of PTSD in patients who experienced the Tsunami plus Earthquake, the Earthquake alone, or neither. (**C**) Kaplan-Meyer 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, β-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,[9,10] 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,[11] 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.[12] Further studies are needed to generalize the present findings to other cohorts.

Acknowledgments

We thank all the CHART-2 study investigators (**Appendix S1**) and the staff of the Department of Evidence-based Cardiovascular Medicine for their contributions.

Funding

This study was supported in part by Grants-in-Aid from a Research Grant from the Ministry of Health, Labour, and Welfare (H.S. and Y.S.) and by a research grant from Banyu Life Science Foundation International (Y.S.).

Conflict of Interest

H.S. received lecture fees from Bayer Yakuhin, Ltd (Osaka, Japan), Daiichi Sankyo Co, Ltd (Tokyo, Japan) and Novartis Pharma K.K. (Tokyo, Japan). The Department of Evidence-based Cardiovascular Medicine, Tohoku University Graduate School of Medicine, is supported in part by the unrestricted research grants from Daiichi Sankyo Co, Ltd (Tokyo, Japan), Bayer Yakuhin, Ltd (Osaka, Japan), Kyowa Hakko Kirin Co, Ltd (Tokyo, Japan), Kowa Pharmaceutical Co, Ltd (Tokyo, Japan), Novartis Pharma K.K. (Tokyo, Japan), Dainippon Sumitomo Pharma, Co, Ltd (Osaka, Japan), and Nippon Boehringer Ingelheim Co, Ltd (Tokyo, Japan).

References

1. 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.
2. Shigemura J, Tanigawa T, Saito I, Nomura S. Psychological distress in workers at the Fukushima nuclear power plants. *JAMA* 2012; **308:** 667–669.
3. 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.
4. 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.
5. 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.
6. 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.
7. 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.
8. 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.
9. 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.
10. 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.
11. 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.
12. 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);
http://dx.doi.org/10.1253/circj.CJ-14-1403