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ORIGINAL ARTICLE

Sex differences in post-traumatic stress disorder in cardiovascular patients after the Great East Japan Earthquake: a report from the CHART-2 Study

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Aims The temporal changes and sex differences in post-traumatic stress disorder (PTSD) after natural disasters remain unclear. Therefore, we examined the prevalence, prognostic impacts, and determinant factors of PTSD after the Great East Japan Earthquake (GEJE) of 11 March 2011 in cardiovascular (CV) patients registered in the Chronic Heart Failure Analysis and Registry in the Tohoku District (CHART)-2 Study ($n = 10\ 219$), with a special reference to sex.

Methods and results By self-completion questionnaires of the Japanese-language version of the Impact of Event Scale–Revised (IES-R-J), the prevalence of PTSD, defined as IES-R-J score ≥25, was 14.8, 15.7, 7.4, and 7.5% in 2011, 2012, 2013, and 2014, respectively. The PTSD rate was higher in women than in men in all years (all $P < 0.01$). During a median 3.5-year follow-up period, the patients with PTSD in 2011 more frequently experienced a composite of all-cause death and hospitalization for acute myocardial infarction, stroke, and heart failure than those without PTSD [adjusted hazard ratio (aHR) 1.27, $P < 0.01$]. Importantly, the prognostic impacts of PTSD on all-cause death (aHR 2.10 vs. 0.87, P for interaction = 0.03) and CV death (aHR 3.43 vs. 0.90, P for interaction = 0.02) were significant in women but not in men. While insomnia medication was a prominent determinant factor of PTSD in both sexes during 2011–14, economic poverty was significantly associated with PTSD only in men.

Conclusion After the GEJE, marked sex differences existed in the prevalence, prognostic impacts, and determinant factors of PTSD, suggesting the importance of sex-sepcific mental stress care in disaster medicine.

Keywords The Great East Japan Earthquake • Mental disorder • Epidemiology • Post-traumatic stress disorder • Prognosis

Introduction

On 11 March 2011, the Great East Japan Earthquake (GEJE), which had a magnitude of 9.0 on the Richter scale and a maximum rating of 7 on the Japanese seismic intensity scale, struck the Tohoku District of Japan.[1–3] The GEJE, followed by a devastating tsunami, destroyed 400 851 houses and killed 19 475 people in the Tohoku District of Japan as of 1 September 2016.[4] Due to the extensive damages by the earthquake, the tsunami and the accidents at the Fukushima Daiichi Nuclear Power Plants, ~400 000 people were forced to evacuate

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into temporary accommodation, whereas of 28 April 2016, ~165 000 people still remain to be evacuated.[5]

Natural disasters and life under evacuation conditions have strong psychological impacts and cause acute stress disorder and post-traumatic stress disorder (PTSD).[6,7] We have recently reported that PTSD that developed after the GEJE was associated with adverse prognosis in patients with cardiovascular disease (CVD).[8] Others previously reported that war veterans with PTSD have an increased risk of death from various causes, including cancer, CVD, and extrinsic causes[9–11] and that women with PTSD were at an increased risk of CVD.[12] To date, however, there are few studies that examined sex differences in PTSD in the same cohort with a long-term follow-up, particularly after natural disasters.

In the present study, we thus examined the prevalence, prognostic impacts, and determinant factors of PTSD and temporal changes in the prevalence and determinant factors of PTSD, with a special reference to sex difference in patients with heart failure (HF) or precursors of HF[13] in the Chronic Heart Failure Analysis and Registry in the Tohoku District-2 (CHART-2) Study.[14–16]

Methods

The CHART-2 Study

The CHART-2 Study was a multicentre, prospective, observational study of Japanese patients with HF (Identifier: NCT00418041) as previously described in detail and was conducted following the ethical principles in the Declaration of Helsinki.[8,14–16] Briefly, the CHART-2 Study enrolled consecutive Japanese patients aged ≥20 years with HF or those with asymptomatic precursors of HF[13,17] between October 2006 and March 2010 in the Tohoku District of Japan ($n = 10\,219$; see Supplementary material).[14–16]

Study design

The protocol of the present study was approved by the ethical committee of the Tohoku University Graduate School of Medicine (#2006-115), and informed consent was obtained from all the patients. The study flow is shown in *Figure 1*. To evaluate PTSD, we employed self-administered questionnaires that included the Japanese-language version of the Impact of Event Scale–Revised (IES-R-J, Cronbach's $\alpha = 0.95$)[18,19] and questions regarding the situations at the time of and after the GEJE. PTSD was defined as a score ≥25.[18,19] In September 2011, we sent the first questionnaires to 8823 patients registered in our CHART-2 Study. Thereafter, we annually sent the IES-R-J questionnaire in September to the patients after excluding those who died or were lost for follow-up in the previous years (*Figure 1*).

In 2011, 2012, 2013, and 2014, we sent questionnaires to 8823, 8187, 7505, and 6733 patients, and 5827 (66%), 5182 (63%), 4525 (60%), and 3930 (58%) returned the responses, respectively (*Figure 1*). Among them, 3620 (41% of total dispatch), 3940 (48%), 3592 (48%), and 3091 (46%) were considered to be valid with complete answers to all questions in 2011, 2012, 2013, and 2014, respectively (*Figure 1*). Finally, 534 (14.8%), 617 (15.7%), 266 (7.4%), and 232 (7.5%) patients were defined as having PTSD in 2011, 2012, 2013, and 2014, respectively.

We compared the prevalence, prognostic impacts, and determinant factors of PTSD and temporal changes in the prevalence and determinant factors of PTSD with a special reference to sex differences and further performed a sub-analysis by HF stages.[13,17] The study outcomes included (i) the composite of all-cause death and hospitalizations for acute myocardial infarction, stroke, and HF; (ii) all-cause death; (iii) cardiovascular (CV) death; (iv) non-CV death; and (v) hospitalization for HF.[8,14–16] We used the time to the first event alone for analysis of the composite endpoint. At least two independent physicians classified causes of death based on death certificates and/or medical records. We did not use diagnostic code [e.g. International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10)] for cause of death and at least two independent physicians classified causes of death based on death certificates and/or medical records. For patients who were only able to obtain dates of death, we defined as unknown cause.

Statistical analysis

All continuous variables are presented as mean (±standard deviation) or median (interquartile range). All categorical variables are presented as frequency (percentage). Welch's *t*-test was used to compare continuous variables, and Fisher's exact test was used to compare categorical variables. The Kaplan–Meier method was used to estimate survival curves, and the log-rank test was utilized to compare survival functions. The competing risk model was also considered, and the Fine and Gray method was adopted to compare cumulative incidence functions.[20] Univariable and multivariable Cox proportional hazard models were used to evaluate risk factors of the study outcomes. The proportional hazards assumption of Cox regression model was tested using the scaled Schoenfeld residuals. Logistic regression analysis was used to assess determinant factors of PTSD in each year from 2011 to 2014. In the multivariable analyses, the stepwise variable selection was adopted to choose the best subsets of covariates. All analyses were performed using R statistical software (version 3.3.0).[21] A P-value <0.05 and a P-value for interaction <0.1 were considered to be statistically significant.

Results

Annual prevalence of post-traumatic stress disorder following the Great East Japan Earthquake

The prevalence of PTSD was significantly higher in women compared with men in all years (all $P < 0.01$) and was significantly decreased in 2013 and 2014 from 2011 and 2012 in both sexes (all $P < 0.01$; *Figure 2A*). In addition, the prevalence of PTSD was highest in patients registered at hospitals in the areas directly affected by the tsunami or within close proximity (<30 km) to the Fukushima Daiichi Nuclear Power Plant facility and was decreased along with a decrease in earthquake intensity experienced in both sexes (*Figure 2B–D*).

Baseline patient characteristics

The patients with PTSD were characterized by higher frequencies of insomnia medication use, tsunami evacuation or trapping, their own hospitalization, injury of close relatives, major property loss, and economic poverty in both sexes and by higher age and higher frequency of unemployment or job change only in men. The baseline characteristics of the patients who returned valid responses in 2012, 2013, and 2014 were similar to those in 2011 (*Table 1*; see Supplementary material online, *Table S1A–C*).

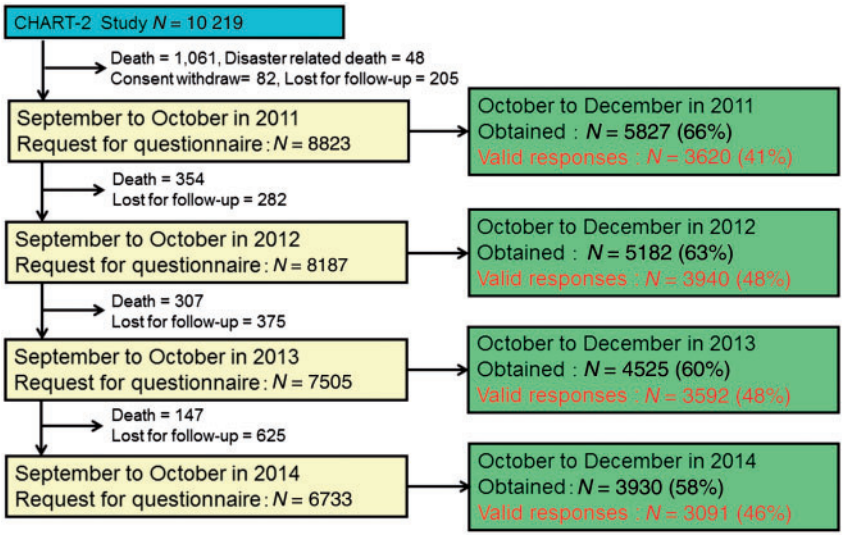

Figure 1 Flowchart of the study.

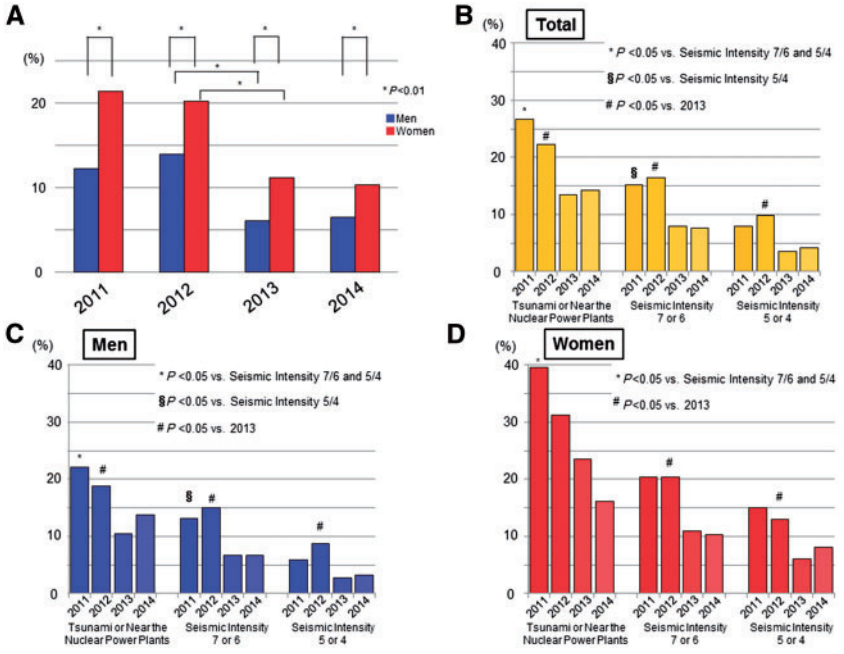

Figure 2 Temporal trend of the prevalence of post-traumatic stress disorder. Temporal change in the prevalence of post-traumatic stress disorder by sex from 2011 to 2014 (*A*). Temporal change in the prevalence of post-traumatic stress disorder from 2011 to 2014 in all heart failure patients (*B*), men (*C*), and women (*D*).

Table 1 Baseline characteristics of the patients who returned valid responses in 2011

Characteristic	Men PTSD			Women PTSD		
	Yes ($n = 328$)	No ($n = 2329$)	*P*-value	Yes ($n = 206$)	No ($n = 757$)	*P*-value
Age, mean (SD) (years)	68.0 (10.7)	66.1 (10.9)	0.002	68.6 (11.4)	68.5 (12.3)	n.s.
Body mass index, mean (SD) (kg/m^2)	24.1 (3.5)	24.2 (4.1)	n.s.	24.0 (5.0)	23.2 (4.4)	0.033
Systolic blood pressure, mean (SD) (mmHg)	129.0 (17.5)	128.0 (17.5)	n.s.	125.1 (19.2)	128.1 (18.4)	0.044
Diastolic blood pressure, mean (SD) (mmHg)	74.2 (11.5)	74.9 (11.2)	n.s.	70.8 (11.1)	72.0 (12.0)	n.s.
Heart rate, mean (SD) (beats/min)	68.6 (13.2)	69.6 (13.3)	n.s.	70.8 (14.0)	72.0 (14.9)	n.s.
Laboratory findings						
LVEF, mean (SD) (%)	60.1 (14.3)	60.5 (13.5)	n.s.	64.5 (13.1)	64.9 (13.6)	n.s.
Haemoglobin, mean (SD) (g/dL)	14.0 (1.63)	13.8 (1.7)	0.010	12.6 (1.4)	12.6 (1.4)	n.s.
Total protein, mean (SD) (g/dL)	7.2 (0.6)	7.2 (0.5)	n.s.	7.2 (0.5)	7.2 (0.6)	n.s.
eGFR, mean (SD) (ml/min/1.73m^2)	65.4 (19.7)	66.2 (18.4)	n.s.	62.8 (20.1)	65.9 (19.8)	n.s.
BNP, median (25th, 75th percentiles) (pg/mL)	60.7 (25.5, 152.2)	49.6 (20.3, 118.0)	n.s.	56.8 (29.4, 140.9)	68.2 (28.8, 162.3)	n.s.
Medical history, *n* (%)						
Heart failure	149 (45.4)	962 (41.3)	n.s.	90 (43.7)	360 (43.1)	n.s.
Admission for heart failure	71 (21.6)	453 (19.5)	n.s.	48 (23.3)	170 (22.5)	n.s.
Hypertension	288 (87.8)	2,017 (86.6)	n.s.	168 (81.6)	609 (80.4)	n.s.
Diabetes mellitus	117 (35.7)	751 (32.2)	n.s.	59 (28.6)	192 (25.4)	n.s.
Atrial fibrillation	101 (31.0)	614 (26.4)	n.s.	55 (26.7)	205 (27.1)	n.s.
Ischaemic heart disease	193 (58.8)	1,467 (63.0)	n.s.	81 (39.3)	305 (40.3)	n.s.
Medication, *n* (%)						
ACE-I or ARB	219 (66.8)	1,541 (66.2)	n.s.	121 (58.7)	435 (57.5)	n.s.
Calcium channel blockers	143 (43.6)	1,091 (46.8)	n.s.	100 (48.5)	334 (44.1)	n.s.
Beta blockers	141 (43.0)	1,018 (43.7)	n.s.	141 (43.0)	1,018 (43.7)	n.s.
Past or current sleep medicines	110 (33.5)	91 (3.9)	<0.001	84 (40.8)	80 (10.6)	<0.001
Disaster experience, *n* (%)						
Tsunami evacuation or trapping	50 (15.2)	108 (4.6)	<0.001	32 (15.5)	36 (4.8)	<0.001
Own hospitalization	20 (6.1)	43 (1.8)	<0.001	23 (11.2)	22 (2.9)	<0.001
Hospitalization of close relatives	58 (17.7)	159 (6.8)	<0.001	44 (21.4)	64 (8.5)	<0.001
Major property loss	153 (46.6)	638 (27.4)	<0.001	85 (41.3)	219 (28.9)	<0.001
Economical poverty	52 (15.9)	72 (3.1)	<0.001	17 (8.3)	24 (3.2)	0.003
Unemployment or job change	18 (5.5)	32 (1.4)	<0.001	4 (1.9)	11 (1.5)	n.s.

ACE-I, angiotensin converting enzyme inhibitors; ARB, angiotensin II receptor blockers; BNP, brain natriuretic peptide; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; PTSD, post-traumatic stress disorder; SD, standard deviation.

Post-traumatic stress disorder and incidence of cardiovascular-related events

Among the 3620 patients who provided valid responses to the questionnaire in 2011, 258 died during the median observation period of 3.5 years after September 2011. Among the deceased patients, 117 (45%) died from CV causes, 110 (43%) from non-CVD, 10 (4%) from extrinsic causes, and the remaining 31 (12%) from unknown causes (see Supplementary material online, *Table S2*). Although there was no significant difference in all-cause mortality between patients with and those without PTSD (8.4 vs. 6.9%, $P = 0.241$), the former tended to have higher incidence of CV death (4.7 vs. 3.0%, $P = 0.055$) and significantly higher incidence of death due to HF (2.8 vs. 1.3%, $P = 0.014$) and that due to acute myocardial infarction (0.9 vs. 0.2%, $P = 0.014$) (see Supplementary material online, *Table S2*). Importantly, female patients with PTSD had higher incidence of CV death, particularly that of HF death, than those without PTSD, which was not noted in male patients (see Supplementary material online, *Table S2*).

Sex differences in prognostic impacts of post-traumatic stress disorder in heart failure patients

Kaplan–Meier estimates for the composite endpoint, all-cause death, CV death, non-CV death, and hospitalization for HF are shown in *Figure 3*. In comparison with HF patients without PTSD, those with PTSD more frequently experienced the composite endpoint [hazard ratio (HR) 1.18; 95% confidence interval (CI) 1.01–1.39, $P = 0.04$; *Figure 3A*] but not that of all-cause death (HR 1.26; 95% CI 0.91–1.74, $P = 0.16$; *Figure 3B*). Similarly, patients with PTSD more frequently experienced the occurrence of CV death when compared with those without it (HR 1.61; 95% CI 1.04–2.52, $P = 0.03$; *Figure 3C*)

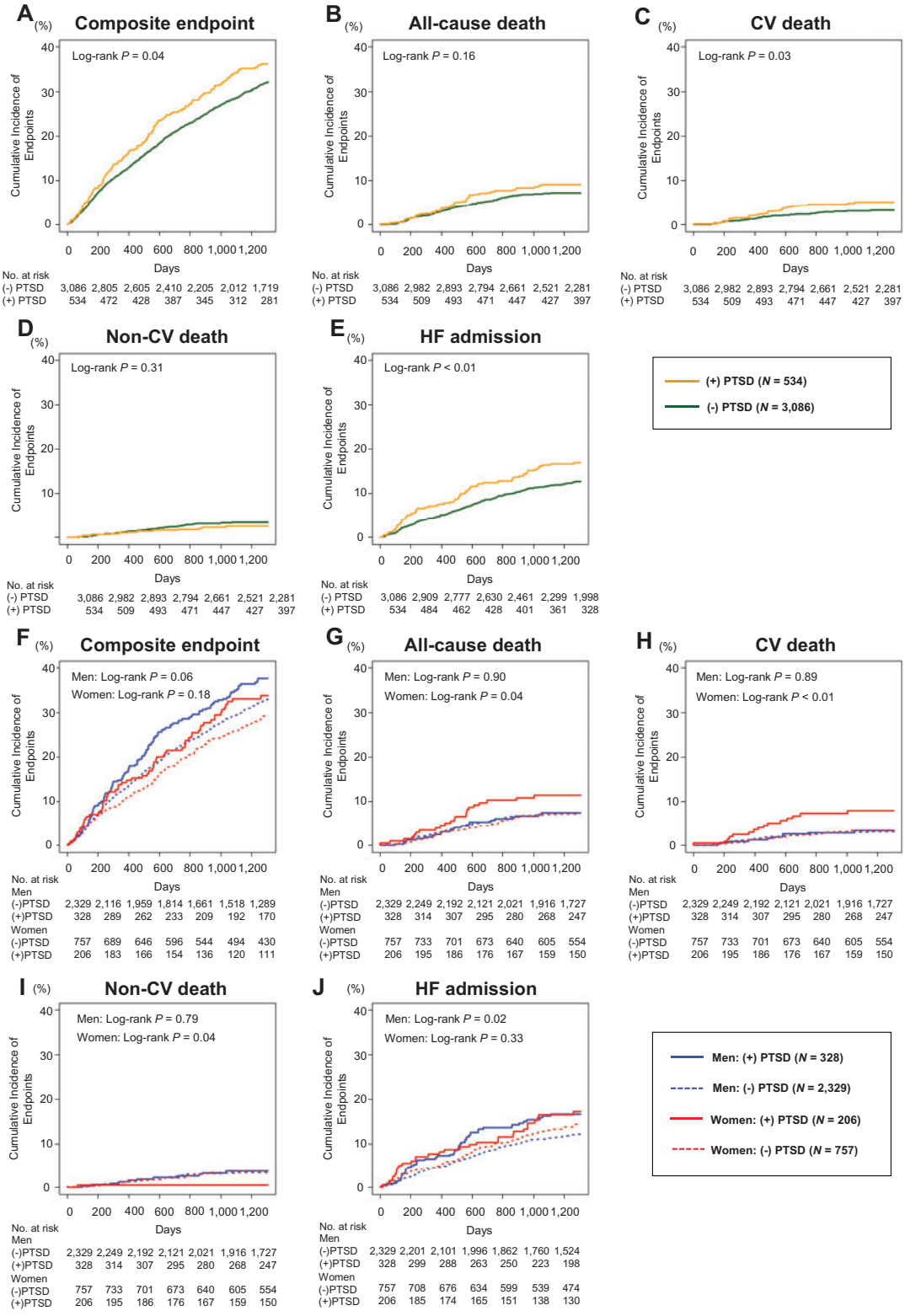

Figure 3 Kaplan–Meier estimates for various endpoints. Kaplan–Meier estimates for the composite endpoint (*A*), all-cause death (*B*), cardiovascular death (CV) (*C*), non-cardiovascular death (*D*), and hospitalization for heart failure (*E*) in all patients. Kaplan–Meier estimates for composite endpoint (*F*), all-cause death (*G*), cardiovascular death (*H*), non-cardiovascular death (*I*), and heart failure (HF) admission (*J*) in men and women.

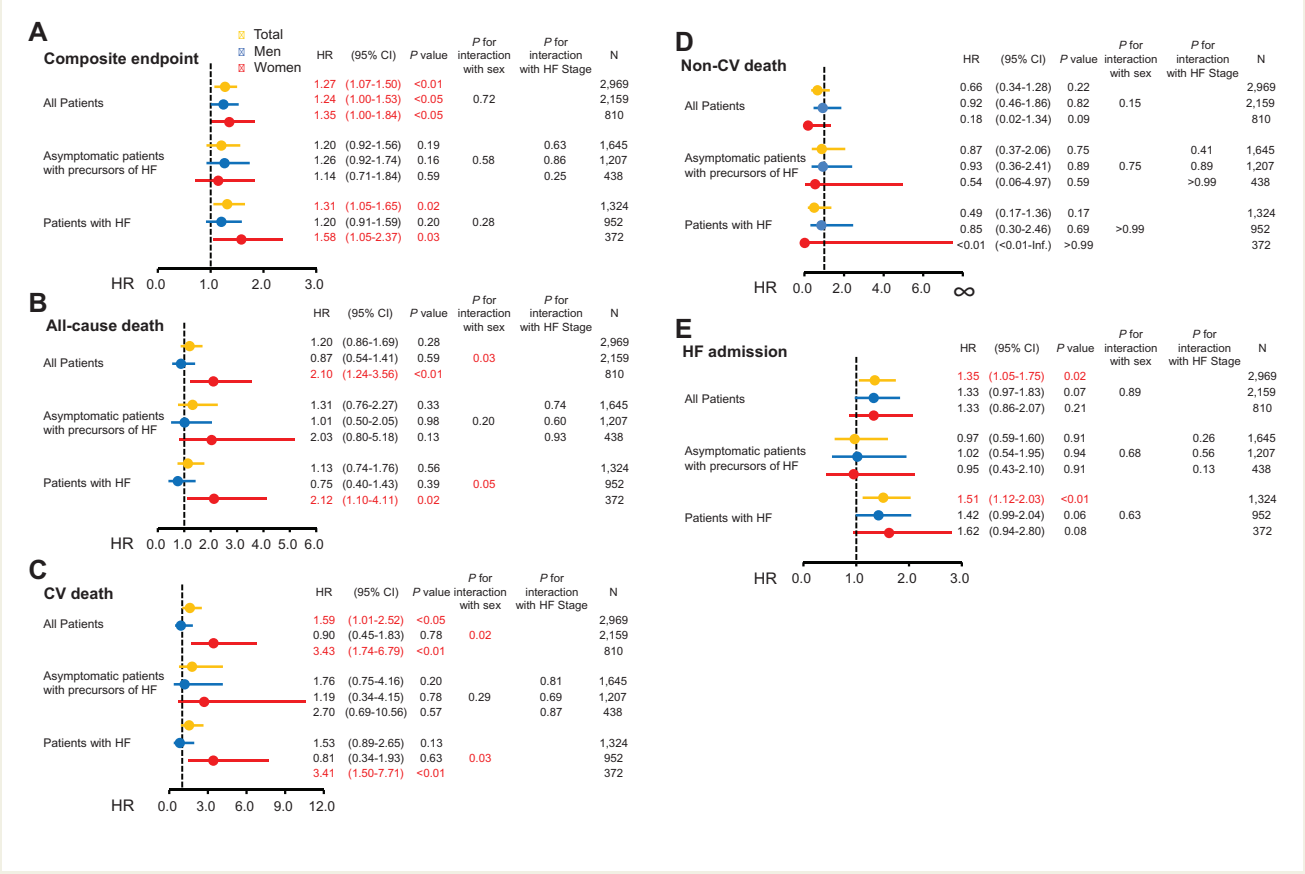

Figure 4 Forest plots for multivariable Cox proportional regression analysis. Forest plots for the composite endpoint (*A*), all-cause death (*B*), cardiovascular death (*C*), non-cardiovascular death (*D*), and heart failure (HF) admission (*E*). Variables used in this analysis were age, sex, heart failure (Stage C/D), systolic blood pressure, diastolic blood pressure, body mass index, history of HF admission, hypertension, diabetes mellitus, brain natriuretic peptide, estimated glomerular filtration rate, left ventricular ejection fraction, atrial fibrillation, cancer, calcium channel blockers, renin–angiotensin system inhibitors, and haemoglobin levels in model (*A*); age, sex, heart failure (Stage C/D), body mass index, systolic blood pressure, diastolic blood pressure, admission for heart failure, brain natriuretic peptide, estimated glomerular filtration rate, left ventricular ejection fraction, atrial fibrillation, renin–angiotensin system inhibitors, and Hb in models (*B*), (*C*), (*D*); age, sex, heart failure (Stage C/D), body mass index, systolic blood pressure, diastolic blood pressure, admission for heart failure, dyslipidaemia, diabetes mellitus, brain natriuretic peptide, estimated glomerular filtration rate, left ventricular ejection fraction, ischaemic heart disease, atrial fibrillation, calcium channel blockers, renin–angiotensin system inhibitors, and haemoglobin in model (*E*). HR, hazard ratio.

but not that of non-CV death (HR 0.73; 95% CI 0.40–1.33, $P = 0.31$; *Figure 3D*). Furthermore, hospitalization rate for HF was significantly higher in patients with PTSD when compared with those without it (HR 1.39; 95% CI 1.09–1.77, $P < 0.01$; *Figure 3E*). Sub-analysis by sex showed that patients with PTSD tended to have increased incidence of the composite endpoint and that of HF admission in men but not in women (*Figure 3F* and *J*). Furthermore, PTSD patients, when compared with those without it, had more increased estimates for cumulative incidence of all-cause death and CV death and more decreased incidence of non-CV death in women but not in men (*Figure 3G–I*). The competing risk model was also considered for CV death, non-CV death, and HF hospitalization, and a result almost identical to the abovementioned was obtained.

The multivariable Cox regression analysis confirmed that PTSD was an independent prognostic factor for the composite endpoint [adjusted HR (aHR) 1.27; 95% CI 1.07–1.50, $P < 0.01$), CV death (aHR 1.59; 95% CI 1.01–2.52, $P < 0.05$) and HF hospitalization (aHR 1.35; 95% CI 1.05–1.75, $P = 0.02$) but not for all-cause death or non-CV death (*Figure 4*). Importantly, subgroup analysis showed that the prognostic impacts of PTSD on all-cause death and CV death were evident in women but not in men, regardless of HF stages, while those on HF admission were mostly attributable to HF patients but not to asymptomatic patients with precursors of HF in both sexes (*Figure 4*). The proportional hazards assumption of Cox regression model was tested using the scaled Schoenfeld residuals. The additive Cox regression model was also considered for the cases in which the proportional hazards assumption were questionable, and a result similar to above was obtained.

Factors related to post-traumatic stress disorder and sex differences

Among the combination of variables selected by the stepwise logistic regression analysis (see Supplementary material online, *Table S3A–D*),

those with significant *P*-values in men, women, or both sexes are shown in *Table 2*. Insomnia medication use was one of the most significant determinant factors of PTSD in all years examined in both sexes (*Table 2*). Economic poverty was a significant determinant factor of PTSD only in men from 2011 to 2014, whereas major property loss was a determinant factor of PTSD in men in 2011 and in women in all years after 2012. Tsunami experience was a significant determinant factor of PTSD from 2011 to 2012 in both sexes, and remained so in 2013 only in women. Among other determinant factors of PTSD, age was a significant factor only in men from 2011 to 2013, injury of themselves in women in 2011 and in men in 2012, and injury of close relatives only in men in 2011 and 2013 (*Table 2*).

Discussion

The major findings of the present study were that (i) among the HF patients, the prevalence of PTSD remained high during the 4-year follow-up after the GEJE, with a decrease from 2012 to 2013 in both sexes; (ii) the prevalence of PTSD was significantly and constantly higher in women than in men; (iii) although the significant adverse impacts of PTSD on the composite endpoint and HF admission were noted in both sexes, those on all-cause death and CV death were evident only in women but not in men; (iv) insomnia medication use was a prominent determinant factor of PTSD after the GEJE in both sexes; and (v) economic poverty was significantly associated with PTSD only in men but not in women, while major property loss was associated with PTSD only in 2011 in men and every year after 2012 in women. These findings demonstrate the significant sex differences in the prevalence, prognostic impacts, and determinant factors of PTSD and temporal changes in those determinant factors, warranting a need for ceaseless mental stress care considering sex differences in CV patients.

Prevalence of post-traumatic stress disorder after the Great East Japan Earthquake

The prevalence of PTSD was noted in up to 15.7% of the patients with CVD in the present study. In a review of 24 studies, the reported prevalence of PTSD after the natural disasters was 12.5%.[6] As a positive association was previously noted between the extent of mental stress and prevalence of PTSD,[22,23] the high prevalence of PTSD in the present study indicates that the GEJE caused enormous mental stress. Indeed, the prevalence of PTSD in the areas exposed to high seismic intensity or directly affected by the tsunami was higher than in other areas.

To the best of our knowledge, this is the first study to examine the prognostic impacts of PTSD in a large cohort study with a special reference to sex differences. The results indicated that the prevalence of PTSD in women was constantly higher than that in men after the GEJE, a consistent finding with the previous study demonstrating that PTSD more frequently occurred in women after a traumatic event.[24] Notably, however, the prevalence of PTSD from 2012 to 2013 reduced significantly in both sexes, regardless of the extent of the disaster, but remained significantly higher in the areas exposed to high seismic intensity and/or the tsunami, particularly in women. These findings suggest that patients who experienced more extensive blow of the disaster may require a longer period of time to recover from PTSD particularly in women when compared with men.

Sex differences in the prognostic impacts of post-traumatic stress disorder

The present study confirmed our preliminary observation that PTSD developed after the GEJE was associated with adverse prognosis in CVD patients[8] with an extended follow-up period. The present findings are clinically important because there are few reports to show the prognostic impacts of PTSD after natural disasters. Furthermore, in the present study, we further examined sex difference in the prognostic impacts of PTSD in the same cohort, which has never been examined regardless of the causes of PTSD. We found that, although both female and male patients with PTSD more frequently experienced CV events than those without it, there were significant sex differences in the endpoints influenced by PTSD, underlining the importance of stratification by sex in evaluating risk factors for CV events.[25] In particular, it should be underlined that PTSD was significantly associated with increased incidence of all-cause and CV death in women but not in men. Thus, female patients, when compared with male patients, appear to have been influenced more severely by PTSD. In contrast, however, we found no sex differences in the adverse impacts of PTSD on HF admission in patients with HF as well as in those with asymptomatic HF precursors. It remains to be elucidated why the sex difference in the impact of PTSD was clearly noted for all-cause death but not for HF admission.

The present study found that PTSD was not associated with an increase in non-CV death, which is not consistent with the previous studies. Boscarino[9] reported that adjusted post-war mortality was associated with PTSD among the Vietnam War veterans after military service not only for CV causes but also for cancer and external causes. It is possible that the difference in the causes of PTSD may explain this discrepancy in the modes of deaths in patients with PTSD. In addition, longer observation period may be needed to evaluate the non-CV mortality risk of PTSD after the GEJE, because influence of PTSD could be evident long after the exposure to the cause of PTSD.[9,26,27] Indeed, Boscarino[9] examined the adjusted post-war mortality in ~30 years after military service. Thus, further follow-up studies are warranted to evaluate the real-world mortality risk of PTSD after the GEJE.

Temporal changes in the factors related to post-traumatic stress disorder and sex differences

In the present study, throughout the 4-year study period, insomnia medication use was a consistent and prominent determinant factor of PTSD after the GEJE in both sexes. Insomnia patients were reported to have higher plasma renin activity and elevated renin and aldosterone levels.[28–31] Insomnia was also found to be an independent predictor of cardiac events in HF patients.[28] As insomnia represents a phenotype of hyperarousal, a major component of PTSD, it is not surprising that insomnia medication use was one of the strongest determinant factors of PTSD, associated with an increased incidence of CV events in the present study.

Unlike insomnia medication use, impacts of other factors on PTSD exhibited temporal changes and showed sex differences, warranting a

Table 2 Factors related to post-traumatic stress disorder and sex differences (2011–2014)

Factor	Adjusted OR (95% CI)	*P*-value	Adjusted OR (95% CI)	*P*-value
A (2011)	Men (*n* = 2159)		Women (*n* = 810)	
Age at questionnaire	1.03 (1.01–1.05)	<0.01	1.01 (0.99–1.03)	n.s.
Systolic blood pressure	1.01 (1.00–1.02)	0.03	0.99 (0.97–1.00)	n.s.
Dyslipidaemia	0.59 (0.41–0.87)	0.01	0.94 (0.59–1.54)	n.s.
Past or current insomnia medication use	8.94 (6.08–13.18)	<0.01	5.08 (3.26–7.93)	<0.01
Tsunami evacuation or trapping	1.88 (1.09–3.17)	0.02	2.06 (1.01–4.12)	0.04
Own hospitalization	1.45 (0.68–2.93)	n.s.	2.74 (1.22–6.06)	0.01
Hospitalization of close relatives	2.06 (1.32–3.18)	<0.01	1.61 (0.91–2.81)	n.s.
Major property loss	1.40 (1.02–1.92)	0.04	1.00 (0.66–1.51)	n.s.
Economical poverty	2.71 (1.61–4.51)	<0.01	1.32 (0.56–2.98)	n.s.
B (2012)	Men (*n* = 2383)		Women (*n* = 877)	
Age at questionnaire	1.02 (1.00–1.03)	0.01	1.00 (0.98–1.02)	n.s.
Haemoglobin	0.90 (0.83–0.98)	0.01	0.93 (0.82–1.06)	n.s.
History of admission for heart failure	0.62 (0.42–0.90)	0.01	1.19 (0.70–2.01)	n.s.
Hypertension	1.54 (1.01–2.42)	<0.05	0.95 (0.56–1.62)	n.s.
ACE-I or ARB	1.39 (1.04–1.87)	0.03	0.72 (0.49–1.07)	n.s.
Calcium channel blocker	0.77 (0.59–1.01)	n.s.	1.57 (1.07–2.34)	0.02
Past or current insomnia medication use	4.86 (3.30–7.12)	<0.01	3.03 (1.95–4.69)	<0.01
Tsunami evacuation or trapping	1.80 (1.05–2.99)	0.03	1.85 (0.86–3.88)	n.s.
Own hospitalization	2.66 (1.31–5.29)	<0.01	0.74 (0.23–2.11)	n.s.
Hospitalization of close relatives	1.30 (0.84–1.99)	n.s.	1.14 (0.62–2.02)	n.s.
Major property loss	1.19 (0.89–1.58)	n.s.	1.52 (1.01–2.28)	0.04
Economical poverty	2.14 (1.23–3.67)	<0.01	1.37 (0.53–3.32)	n.s.
C (2013)	Men (*n* = 2182)		Women (*n* = 788)	
Age at questionnaire	1.03 (1.01–1.06)	<0.01	1.01 (0.98–1.04)	n.s.
Systolic blood pressure	1.01 (1.00–1.02)	0.03	0.99 (0.97–1.00)	n.s.
Dyslipidaemia	0.59 (0.41–0.87)	0.01	0.94 (0.59–1.54)	n.s.
Past or current insomnia medication use	5.46 (3.34–8.81)	<0.01	4.80 (2.65–8.66)	<0.01
Tsunami evacuation or trapping	1.51 (0.67–3.16)	n.s.	4.85 (1.81–12.79)	<0.01
Own hospitalization	0.24 (0.01–1.26)	n.s.	0.72 (0.09–3.86)	n.s.
Hospitalization of close relatives	1.87 (1.05–3.19)	0.03	0.67 (0.26–1.57)	n.s.
Major property loss	1.39 (0.90–2.13)	n.s.	1.71 (0.96–3.01)	0.06
Economical poverty	2.90 (1.46–5.56)	<0.01	0.50 (0.10–1.80)	n.s.
D (2014)	Men (*n* = 2534)		Women (*n* = 637)	
Age at questionnaire	1.02 (1.00–1.05)	n.s.	1.02 (0.99–1.05)	n.s.
eGFR	0.99 (0.98–1.00)	n.s.	0.98 (0.96–0.99)	0.01
Beta blockers	1.17 (0.76–1.79)	n.s.	2.21 (1.17–4.18)	0.01
Past or current insomnia medication use	6.20 (3.68–10.35)	<0.01	2.41 (1.24–4.59)	0.01
Tsunami evacuation or trapping	1.33 (0.59–2.81)	n.s.	0.75 (0.22–2.24)	n.s.
Own hospitalization	1.37 (0.31–4.49)	n.s.	1.45 (0.35–5.36)	n.s.
Hospitalization of close relatives	1.80 (0.96–3.23)	n.s.	1.09 (0.44–2.47)	n.s.
Major property loss	1.30 (0.83–2.00)	n.s.	1.90 (1.01–3.50)	0.04
Economical poverty	2.20 (1.00–4.67)	<0.05	1.96 (0.55–6.17)	n.s.

ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; CI, confidence interval; eGFR, estimated glomerular filtration rate; OR, odds ratio.

need for the different mental stress care by sex. Economic poverty was strongly associated with PTSD after the GEJE from 2011 to 2014 in men but not in women. In addition, major property loss was a significant determinant factor of PTSD in men only in 2011 but was associated with PTSD in women every year after 2012. Thus, economic loss might have affected men more than women soon after the GEJE, but later affected women longer after it. Thus, it is possible that relocation due to major property loss after the GEJE might have caused the later development of PTSD in women, since a previous study reported that relocation was associated with mood disorders in women.[32]

Study limitations

Several limitations should be mentioned for the present study. First, although we used the clinical data of age, medical history, co-morbidity, and history of insomnia obtained at the time of the GEJE, we used the data for the blood biochemical and echocardiographic information obtained at the time of entry into the CHART-2 Study. Furthermore, we did not consider possible changes in these data after 2011. Second, the self-reported IES-R-J score was used to determine the presence or absence of PTSD. Although the IES-R-J score, which examines the presence and intensity of post-traumatic stress symptoms, has been established as a reliable score for PTSD,[18,19] the diagnosis was made without an interview by psychiatrists. Third, we were unable to follow-up some patients after the GEJE, mainly due to their displacement and need to evacuate following the GEJE. As these patients would be expected to have a higher prevalence of PTSD, the present results might have underestimated the PTSD prevalence. Relatively low response rates for the questionnaire might have biased our findings. For example, there is a concern that the study population did not necessarily represent the whole population in the disaster area, which could influence the classification and estimation of the prevalence for PTSD, other mental health issues, and somatic diseases directly related to the study outcomes. Finally, caution should be taken when generalizing the present findings to other populations, because the CHART-2 Study is a prospective observational study with Japanese HF patients.

Conclusions

The present study of the GEJE demonstrated that there were marked sex differences in the prevalence, prognostic impacts, and determinant factors of PTSD and temporal changes in determinant factors. Thus, in CV patients after a disaster, ceaseless mental stress care considering sex differences of related factors of PTSD is needed for early detection and therapeutic intervention for mental stress, by which the prognosis of the patients with PTSD may improve.

Supplementary material

Supplementary material is available at *European Heart Journal – Quality of Care and Clinical Outcomes* online.

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