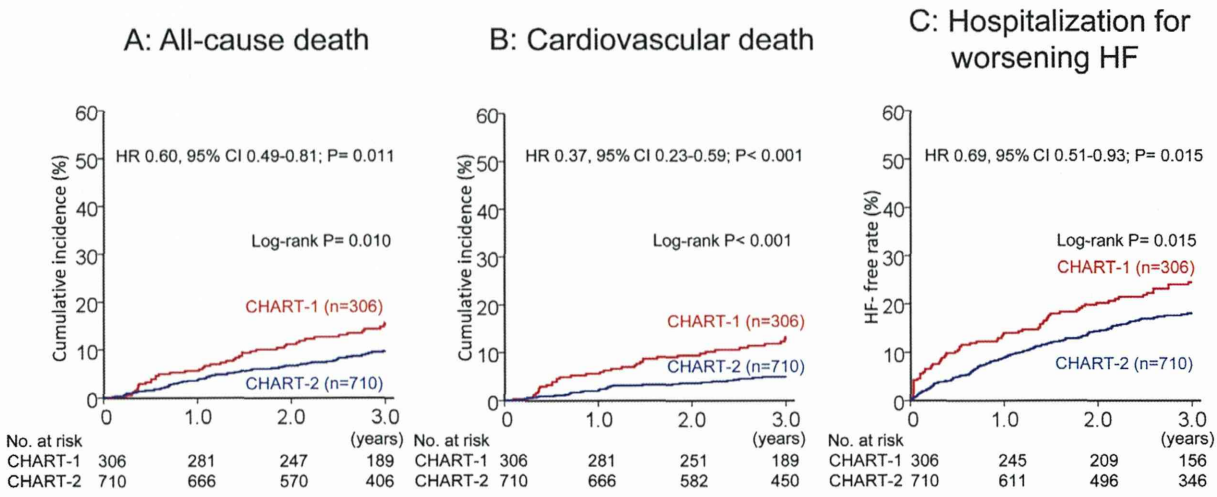


Figure 1. Kaplan-Meier survival curves for (**A**) all-cause death, (**B**) cardiovascular death and (**C**) hospitalization for worsening heart failure (HF).

several covariates were estimated using the Cox proportional hazard model, including interaction terms using the same variables chosen with the stepwise method. P-value for interaction <0.1 was considered to be statistically significant. All calculations were performed using SPSS 22.0 for Windows and R version 3.0.2.

Results

Baseline DCM Patient Characteristics

There were no significant differences in age, prevalence of male sex, heart rate, blood pressure or any other laboratory findings between the CHART-1 and the CHART-2 Studies (**Table 1**). In the echocardiography data, LVEF was more preserved and LVDd and LV end-systolic diameter were smaller in the CHART-2 patients. The prevalence of hypertension, dyslipidemia and diabetes mellitus was all increased from CHART-1 to CHART-2. While RASI use was similar at enrollment, the use of β-blockers and aldosterone antagonists was increased and use of loop diuretics and digitalis was decreased in CHART-2. Implantable cardioverter defibrillator/cardiac resynchronization therapy defibrillator (ICD/CRT-D) were more frequently used in CHART-2.

Incidence of Death and HF in DCM Patients

A total of 106 patients died during the 3-year follow-up (44 in CHART-1 and 62 in CHART-2). Crude 3-year mortality was significantly decreased from 14% in CHART-1 to 9% in CHART-2 (hazard ratio [HR], 0.60; 95% CI: 0.49–0.81, P=0.011; **Figure 1A**). Three-year cardiovascular death rate was also improved from 12% (n=32) in CHART-1 to 4.5% (n=37) in CHART-2 (HR, 0.37; 95% CI: 0.23–0.59, P<0.001; **Figure 1B**). Hospitalization for worsening HF was noted in 184 patients (69 in CHART-1 and 115 in CHART-2). Three-year HF admission rate was significantly decreased from 23% in CHART-1 to 16% in CHART-2 (HR, 0.69; 95% CI: 0.51–0.93, P=0.015; **Figure 1C**). After adjustment of the following variables, including systolic blood pressure, hypertension, age, LVEF, BNP, BMI, eGFR, β-blocker, and aldosterone antagonist, HR for each category was as follows: all-cause death, HR=0.60 (95% CI: 0.34–1.04, P=0.069), cardiovascular death, HR=0.26 (95% CI: 0.14–0.50, P<0.001) and HF admission, HR=0.90 (95% CI: 0.59–1.37, P=0.632).

Mode of Death in DCM Patients

Among the total 44 deaths in the CHART-1 Study, there were 37 cardiovascular deaths (84.1%) and 5 non-cardiovascular deaths (11.4%; **Figure 2**). The causes of the remaining 2 deaths were unknown. Among the total 62 deaths in CHART-2, 32 (51.6%) were cardiovascular deaths and 23 (37.1%) were non-cardiovascular deaths, while the causes of the remaining 7 deaths were unknown. Among the cardiovascular deaths, sudden death rate was significantly decreased from 5.2% in CHART-1 to 0.4% in CHART-2 (P<0.001). Incidence of death due to HF (from 5.6% to 3.2%, P=0.062) and stroke (from 1.0% to 0.4%, P=0.257) was non-significantly decreased, whereas non-cardiovascular death rate tended to increase (from 1.6% to 3.2%, P=0.107).

Predictors of All-Cause Death

Table 2 list the results of the multivariate Cox proportional hazard model for all-cause death. In CHART-1, 4 variables (age >70 years, NYHA III/IV, BNP ≥220 pg/ml and aldosterone antagonist) were selected using the stepwise multivariate Cox model, in which BNP ≥220 pg/ml and the use of aldosterone antagonist were significantly associated with all-cause death (**Table 2A**). In CHART-2, 7 variables (hypertension, age >70 years, LVEF ≤40%, BNP ≥220 pg/ml, BMI <18.5 kg/m^2, eGFR ≤50 ml·min^{-1}·1.73 m^{-2} and β-blocker) were selected, and hypertension, age >70 years, LVEF ≤40%, BNP ≥220 pg/ml and β-blocker were significantly associated with all-cause death. The final model identified several factors that were significantly associated with decreased incidence of 3-year death, including NYHA III/IV, age ≥70 years, BNP ≥220 pg/ml, BMI <18.5 kg/m^2 and use of aldosterone antagonist in the CHART-1 Study, and age ≥70 years, BNP ≥220 pg/ml, eGFR <50 ml·min^{-1}·1.73 m^{-2}, and LVEF ≤40% in the CHART-2 study (**Table 2B**). We further examined the differences in

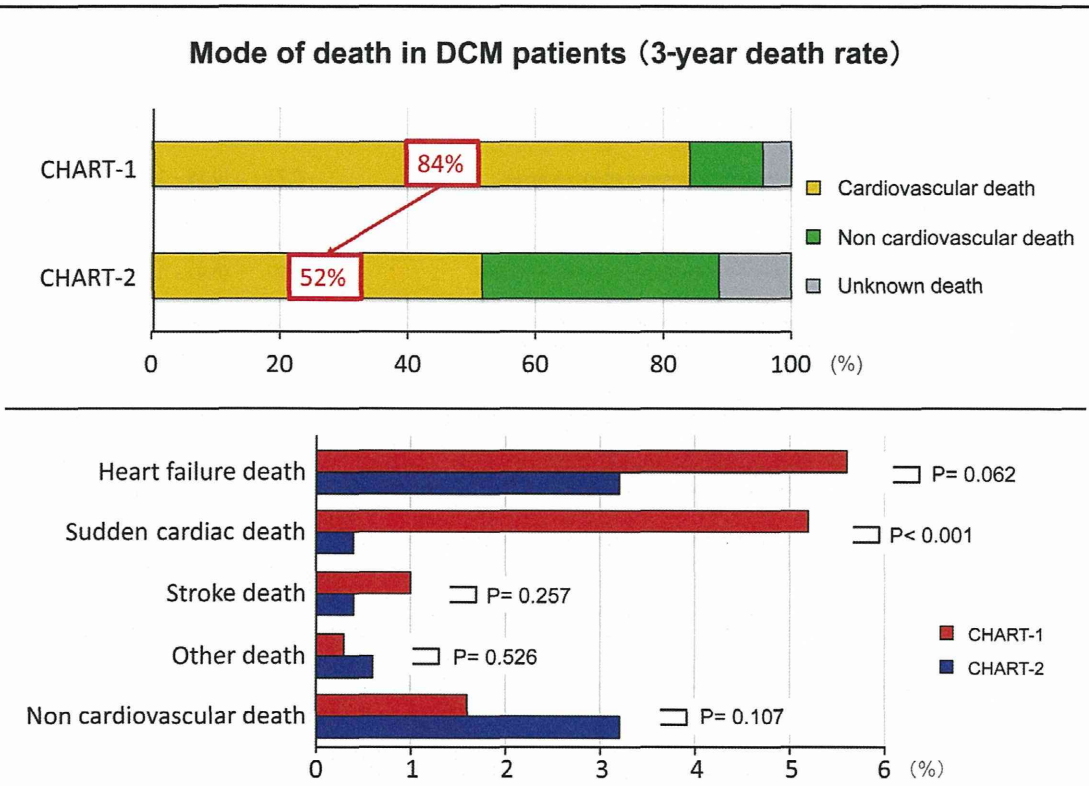
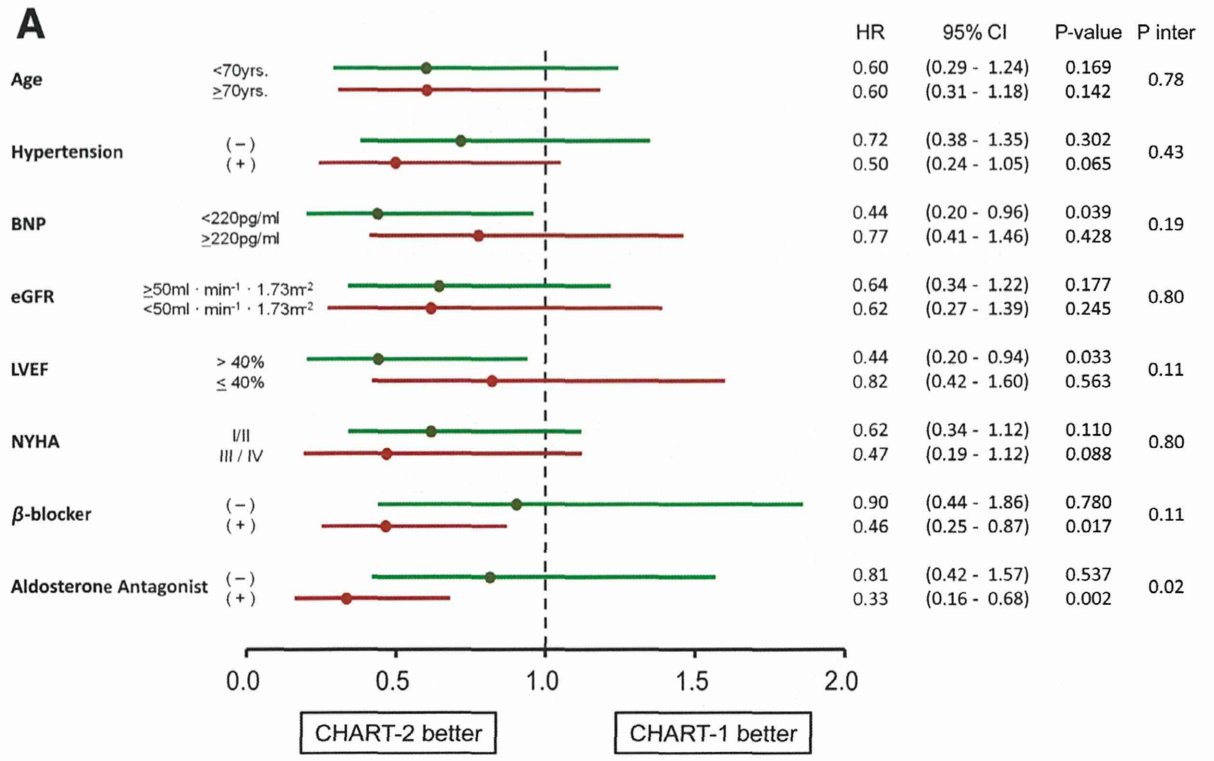


Figure 2. Mode of death in dilated cardiomyopathy (DCM) patients (3-year death rate).

Table 2. Prognostic Factors of All-Cause Death in DCM Patients

All-cause death (3-year death)	CHART-1			CHART-2		
	HR	95% CI	P-value	HR	95% CI	P-value
A. Multivariate Cox models by using stepwise method						
Age ≥70 years	2.25	1.01–4.98	0.046	1.85	1.06–3.25	0.032
BNP <220 pg/ml	0.37	0.16–0.84	0.017	0.21	0.11–0.40	<0.001
Aldosterone antagonists	4.64	2.15–9.99	<0.001			
NYHA III/IV	2.21	0.94–5.18	0.068			
Hypertension				0.48	0.28–0.84	0.010
LVEF >40%				0.49	0.27–0.91	0.023
BMI <18.5 kg/m^2				1.89	0.90–3.99	0.094
eGFR ≤50 ml·min^{-1}·1.73 m^{-2}				1.72	0.95–3.12	0.072
β-blockers				0.34	0.19–0.61	<0.001
B. Multivariate Cox models						
Hypertension	0.82	0.39–1.72	0.604	0.52	0.30–0.91	0.021
NYHA III/IV	2.47	1.12–5.43	0.024	1.19	0.63–2.27	0.587
Age ≥70 years	2.72	1.32–5.58	0.006	1.81	1.04–3.16	0.037
BMI <18.5 kg/m^2	0.12	0.02–0.91	0.040	1.94	0.92–4.11	0.082
BNP <220 pg/ml	0.39	0.18–0.85	0.018	0.22	0.12–0.41	<0.001
eGFR ≤50 ml·min^{-1}·1.73 m^{-2}	1.81	0.86–3.80	0.116	1.83	1.01–3.33	0.047
LVEF >40%	1.12	0.54–2.38	0.749	0.52	0.28–0.97	0.040
β-blockers	0.87	0.42–1.86	0.700	0.35	0.19–0.64	0.001
Aldosterone antagonists	3.18	1.59–6.35	<0.001	1.34	0.78–2.31	0.295

HR, hazard ratio. Other abbreviations as in Table 1.



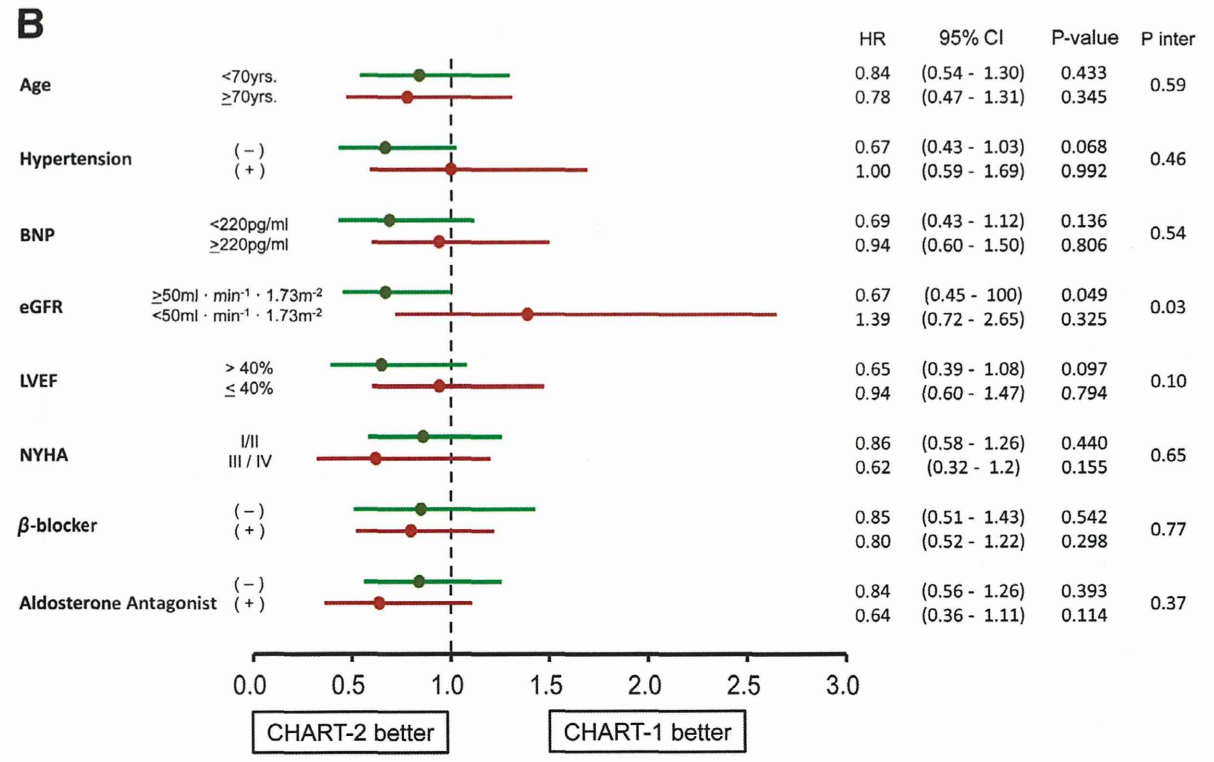


Figure 3. Forest plots for (**A**) overall survival and (**B**) incidence of heart failure in each subgroup (multivariate Cox proportional hazard model). BNP, brain natriuretic peptide; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association.

Table 3. Prognostic Impact of Medications in DCM Patients

All-cause death (3-year death)	HR	95% CI	P-value
A. β-blockers			
All patients (n=1,016)			
Overall	0.59	0.41–0.88	0.009
IPTW	0.65	0.48–0.89	0.007
CHART-1 (n=306)			
Overall	0.94	0.52–1.70	0.838
IPTW	1.42	0.78–2.59	0.254
CHART-2 (n=710)			
Overall	0.52	0.30–0.88	0.015
IPTW	0.61	0.42–0.87	0.006
B. Aldosterone antagonists			
All patients (n=1,016)			
Overall	1.75	1.20–2.57	0.004
IPTW	1.62	1.19–2.20	0.002
CHART-1 (n=306)			
Overall	3.28	1.81–5.96	<0.001
IPTW	4.55	2.44–8.47	<0.001
CHART-2 (n=710)			
Overall	1.45	0.88–2.39	0.144
IPTW	1.20	0.83–1.72	0.332

DCM, dilated cardiomyopathy; IPTW, inverse probability weighting.

3-year mortality between CHART-1 and CHART-2 in the subgroups according to the cut-offs used in the Cox model. As a result, 3-year survival was better in CHART-2 in patients with BNP <220 pg/ml, LVEF >40%, using β-blockers and aldosterone antagonists (**Figures S1,3A**). In contrast, the incidence of HF hospitalization was similar between the CHART-1 and the CHART-2 Studies except for patients with reduced eGFR (**Figure 3B**).

On IPTW analysis using the propensity score, β-blocker use was independently associated with a lower mortality in the total population (HR, 0.65; 95% CI: 0.48–0.89; P=0.007) and in 710 patients from the CHART-2 Study (HR, 0.61; 95% CI: 0.42–0.87; P=0.006), but not in 306 patients from the CHART-1 Study (HR, 1.42; 95% CI: 0.78–2.59; P=0.254; **Table 3A**). In contrast, on IPTW analysis, aldosterone use was associated with increased mortality in the total population and in the CHART-1 Study, but not in the CHART-2 Study (**Table 3B**). In patients with LVEF >40%, IPTW analysis suggested no prognostic effect of β-blocker use in both the CHART-1 and the CHART-2 Studies (P-value for interaction=0.68), while in patients with LVEF ≤40%, β-blocker use was associated with better survival in the CHART-2, but not in the CHART-1 Study (P-value for interaction <0.01; **Figure 4**). IPTW analysis also suggested the prognostic benefits of β-blocker use in the CHART-2, but not in the CHART-1, Study, regardless of subgroup classification according to BNP level or aldosterone antagonist use (**Figure 4**).

Discussion

The novel findings of the present study are that (1) 3-year mortality of Japanese DCM patients has recently improved; (2) evidence-based medication for CHF has been implemented in Japan; (3) prevalence of lifestyle comorbidities (eg, hypertension, hyperlipidemia and diabetes mellitus) has been increasing in Japanese DCM patients; and (4) improvement in long-term prognosis of DCM patients was noted in the patients with BNP <220 pg/ml, LVEF >40%, β-blocker use and aldosterone antagonist use.

Improved Long-Term Prognosis of Japanese DCM Patients

The present study demonstrates that the crude 3-year incidence of all-cause death, cardiovascular death and admission for HF were all significantly decreased in the CHART-2 Study compared with the CHART-1 Study. In particular, 3-year mortality was decreased by approximately 40%, from 14% (4.6%/year) in the CHART-1 to 9% (3%/year) in the CHART-2 Study. Indeed, evidence-based medication for CHF has been implemented in Japan with the resultant improvement in long-term prognosis. The prescription rates of RASI, β-blockers and aldosterone antagonists were all increased in the CHART-2 compared with the CHART-1 Study. Thus, it is possible that the implementation of these evidence-based medications has contributed to the improvement of long-term mortality of DCM patients in the present study. This trend, along with increased use of RASI and β-blockers, is consistent with the previous report that 5-year mortality of DCM patients was decreased from 41% (8%/year) in 1982–1989 to 19% (3.8%/year) in 1990–2002 in Japan.[2] The present study further demonstrates that the trend of improvement in long-term prognosis of DCM patients has continued in the last 10 years in Japan.

Factors Contributing to Improvement of Long-Term Prognosis

In the present study with DCM patients, the CHART-2 patients had better clinical background, including LV function, compared with the CHART-1 patients, which might have contributed in part to the improved prognosis of the CHART-2 patients. Indeed, after adjustment for clinical background selected in the stepwise Cox regression analysis, the decreased incidence of all-cause death and HF admissions in the CHART-2 Study became insignificant, although there was a

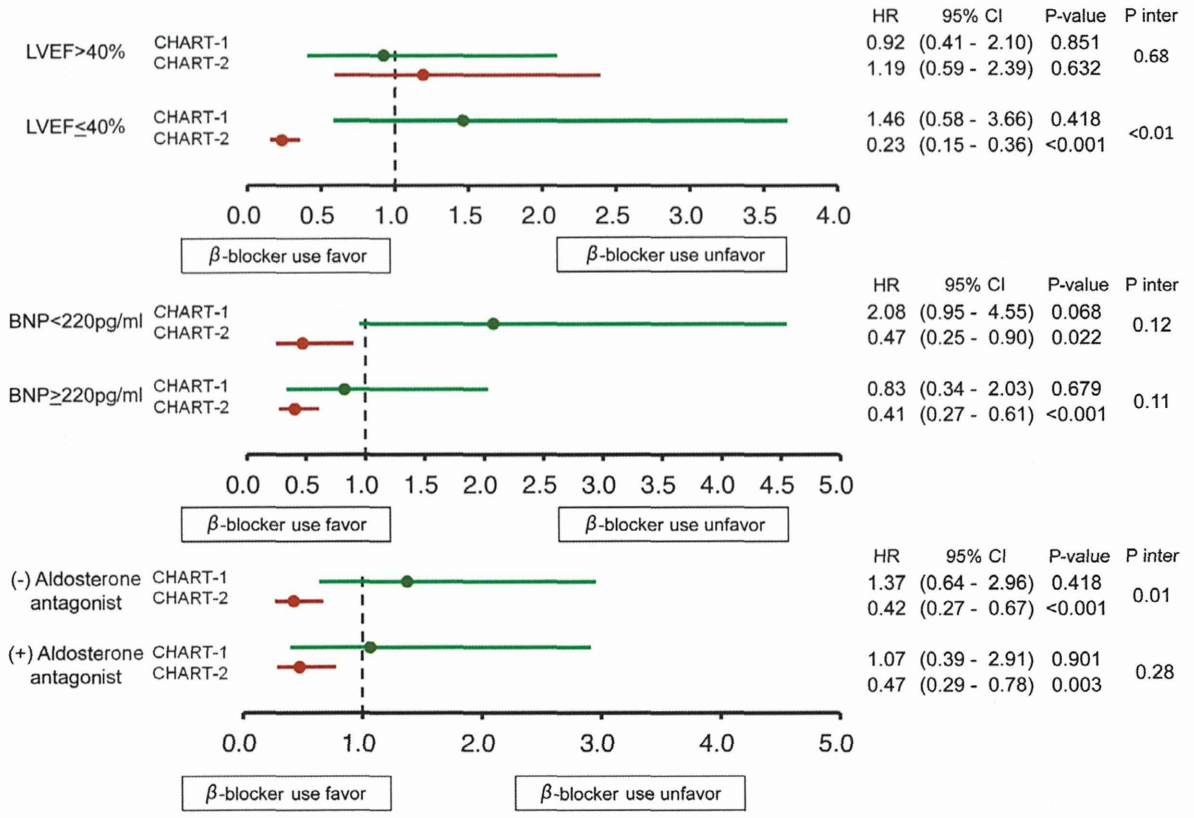


Figure 4. Inverse probability of treatment weighting analysis for each subgroup. BNP, brain natriuretic peptide; LVEF, left ventricular ejection fraction.

tendency for improved all-cause death (adjusted HR, 0.61; P=0.054) and the decreased incidence of cardiovascular death remained significant even after the adjustment (adjusted HR, 0.29; P<0.001). This finding, however, could be explained by the benefits of implementation of evidence-based medication, particularly, by that of β-blockers. In the present study, the use of β-blockers was markedly increased from 49% in CHART-1 to 81% in CHART-2, and the DCM patients treated with β-blockers had a better prognosis than those without them. Furthermore, the decrease in all-cause mortality was mainly associated with a decrease in cardiovascular death, specifically sudden death, supporting the notion that β-blockers were effective in improving the long-term prognosis of DCM patients in the present study. This is consistent with the previous reports that β-blockers improved LVEF and all-cause mortality in patients with CHF.[19–22] In addition, it is speculated that not only the prescription rates but also the dose of β-blockers was increased from the CHART-1 to the CHART-2 Studies, resulting in reduced mortality. Furthermore, it is conceivable that ICD/CRT-D treatment also played a significant role in preventing sudden cardiac death in the CHART-2 Study, although it is difficult to demonstrate its efficacy due to the small number of patients treated with ICD/CRT-D in the present study.

Subgroups With Improved Long-Term Prognosis

The present study demonstrated that the long-term prognosis of DCM patients was improved in several subgroups. In particular, the improvement was noted in patients with LVEF >40%, but not in those with LVEF ≤40%. It is difficult to explain the reason for this finding with regard to β-blocker use, because on IPTW analysis β-blockers improved prognosis over time from CHART-1 to CHART-2 in patients with LVEF ≤40% but not in those with LVEF >40%. This finding, however, is consistent with the previous findings that in-hospital mortality was improved over time between 2005 and 2010 in HF patients with preserved LVEF, but not in those with reduced LVEF,[23] and that HF patients with recovered LVEF had better prognosis than those with reduced LVEF or near-normal LVEF.[24,25] Furthermore, the present study also showed that the improvement was noted in the subgroup with BNP <220 pg/ml and that with aldosterone antagonist use. Interestingly, β-blocker use was associated with improved mortality in these subgroups, but not in those with BNP ≥220 pg/ml or those without aldosterone antagonist use, although the P-values for interaction were not significant. Thus, appropriate use of β-blockers might have played a role in the improvement of mortality in patients with BNP <220 pg/ml and in those with aldosterone antagonist use.

Increase in Lifestyle-Related Comorbidities

Another novel finding of the present study is that the prevalence of lifestyle-related comorbidities (eg, hypertension, dyslipidemia and diabetes mellitus) was increased from the

CHART-1 to the CHART-2 Study. The recent trend of westernization of clinical background in overall CHF patients in Japan has been previously reported,[7,9] and lifestyle-related diseases are emerging as comorbidities in DCM patients in Japan. Given that hypertension, dyslipidemia and diabetes are all recognized as coronary risk factors, this suggests that ischemic heart disease may stand out as one of the main causes of mortality and morbidity in DCM patients in the near future. Thus, more attention should be paid to the prevention of coronary artery disease through management of lifestyle-related comorbidities in current DCM practice.

Study Limitations

Several limitations should be mentioned for the present study. First, given that both the CHART-1 and CHART-2 Studies are prospective observational studies in the Tohoku district of Japan, we need to be cautious when extrapolating the present findings to other cohorts, particularly to those in other countries. Second, the diagnosis, evaluation, and management of DCM were made in each participating hospital, and thus there could be a selection and/or other bias in the present study. Finally, the number of the patients enrolled from the CHART-1 Study was relatively small, which might have limited the power to identify significant observations.

Conclusions

Three-year mortality of DCM patients has been significantly improved along with the implementation of evidence-based medication in Japan. Subgroup analysis, however, suggested that the improvement was concentrated in the subgroups with BNP <220 pg/ml, LVEF >40%, β-blocker use and aldosterone antagonist use.

Acknowledgments

We thank all members of the Tohoku Heart Failure Society and staff of the Department of Evidence-based Cardiovascular Medicine for their kind contributions (**Appendix**). This study was supported by Grants-in-Aid from a Research Grant from the Ministry of Health, Labour, and Welfare (Y.S., H.S.).

Disclosures

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

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Supplementary Files

Supplementary File 1

Figure S1. Change in survival rate between CHART-1 and CHART-2 for (**A**) left ventricular ejection fraction (LVEF) > or ≤40%, (**B**) brain natriuretic peptide (BNP) < or ≥220 pg/ml, (**C**) presence of β-blockers and (**D**) presence of aldosterone antagonist.

Please find supplementary file(s);
http://dx.doi.org/10.1253/circj.CJ-14-0939

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 –

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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

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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/m^2	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·min^{-1}·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.

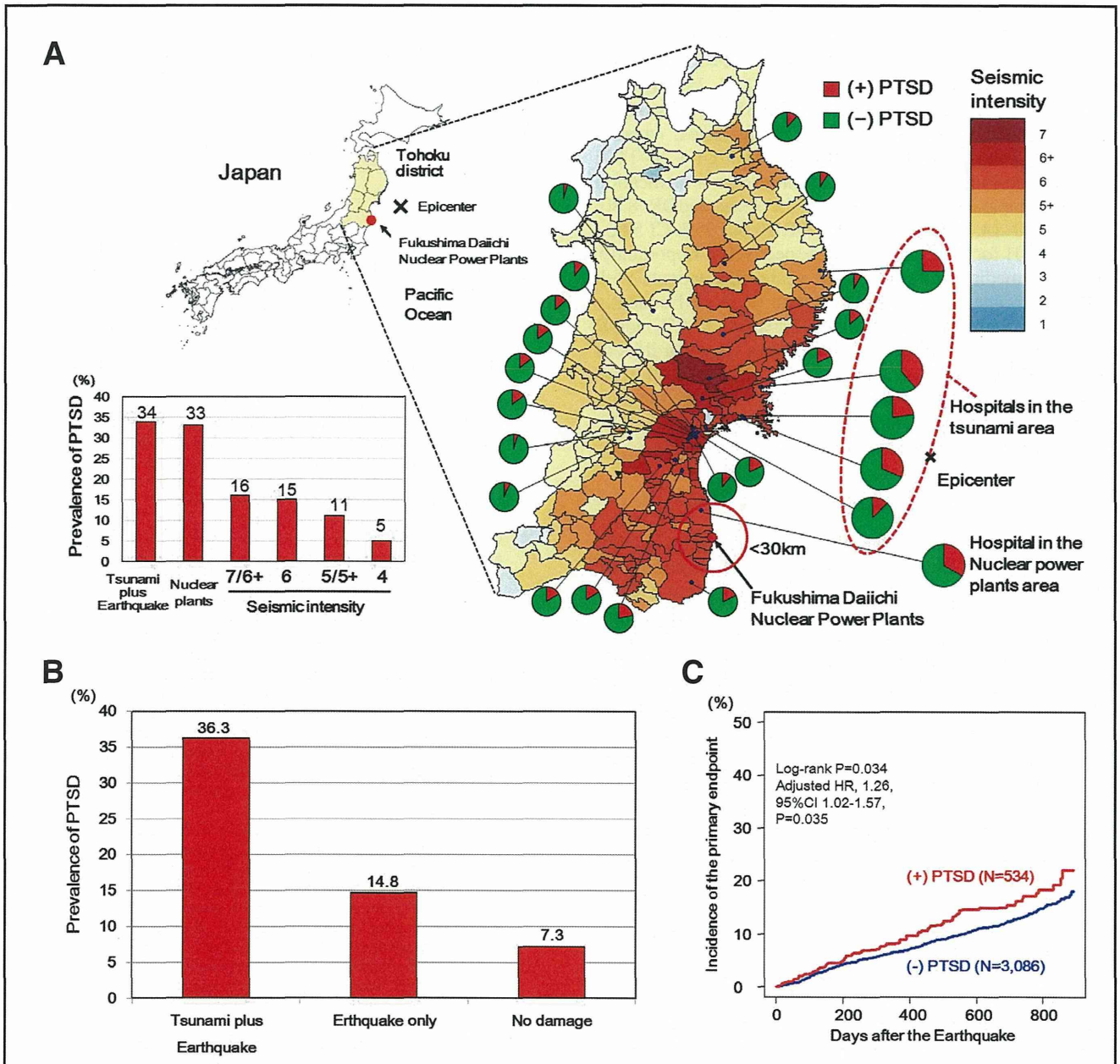

Figure. (**A**) Location of the epicenter of the Great East Japan Earthquake, the Fukushima-Daiichi nuclear power plants, and the study sites, and the proportions of patients with post-traumatic stress disorder (PTSD). (**B**) The questionnaire-based prevalence of PTSD in patients who experienced the 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 (<30 km) 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