



Original article

Gender differences in prognostic relevance of self-care behaviors on mortality and hospitalization in patients with heart failure – A report from the CHART-2 Study



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ABSTRACT

Background: Self-care behaviors (ScB) are associated with symptoms and outcomes in patients with heart failure (HF). However, little is known about gender differences in the prognostic relevance of ScB in HF patients.

Methods: We examined gender differences in ScB of HF patients regarding its prognostic associations with mortality and HF hospitalization with a reference to ScB dimensions. The European Heart Failure Self-Care Behavior Scale (EHFScBS) was used to evaluate ScB in 2233 patients with Stage C/D HF in the CHART-2 Study.

Results: Male patients ($n = 1583$) were younger (71 vs. 73 yrs) and had lower ScB (median 33 vs. 31) (all $p < 0.001$) than females ($n = 650$). During the median follow-up of 2.57 years, patients with high ScB (score 12–32, $n = 1090$), as compared with low ScB patients (score 33–60, $n = 1143$), had significantly increased all-cause mortality in males [adjusted hazard ratio (aHR) 1.44, $p = 0.02$] but not in females (aHR 0.80, $p = 0.40$) (p for interaction 0.02), while ScB was not significantly associated with incidence of HF hospitalization in both genders. Among the 3 dimensions in EHFScBS, complying with regimen was associated with decreased mortality in females, but not in males (p for interaction 0.003), while asking for help was related with increased incidence of HF hospitalization in males (aHR 1.34, $p = 0.072$) but not in females (aHR 0.98, $p = 0.931$) (p for interaction 0.048).

Conclusions: There were gender differences in the prognostic relevance of self-care with mortality and incidence of HF hospitalization, suggesting that self-care should be implemented considering gender differences to improve prognosis.

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Introduction

Along with the aging of the societies, the number of patients with heart failure (HF) has been increasing worldwide, and has been termed an “HF pandemic” [1,2]. However, despite significant

progresses in the management of HF including evidence-based pharmacological management [3–5], HF patients are still distressed with symptoms, limited functional capacity, poor quality of life (QOL), and increased mortality [1,2,6].

Self-care behaviors (ScB) are associated with symptoms and outcomes in HF patients. Non-compliance with medication, diet, or fluid restriction decreases the efficacy of the treatment prescribed and exposes the patient to clinical destabilization, which can lead to increased HF symptoms [7]. Non-adherence to salt and water restriction is one of the leading causes of rehospitalization in Japanese patients with HF [8,9]. Furthermore, lack of improvement in

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health-related QOL after discharge from the hospital is a powerful predictor of rehospitalization and mortality [10]. These lines of evidence suggest the importance of ScB management for patients and clinicians to improve HF symptoms and, in turn, reduce high rates of mortality and hospitalization. Indeed, a previous meta-analysis demonstrated that HF management programs aimed at promoting self-care reduced rehospitalization rates and mortality [11]. However, limited data are available regarding the relationships between ScB and prognosis in HF patients [12,13], particularly with a reference to ScB dimensions, such as (1) complying with a regimen for medication, diet, and exercise, (2) monitoring symptoms, and (3) seeking assistance when symptoms occur [14,15]. Furthermore, few studies have addressed gender differences in the prognostic relevance of ScB with mortality and hospitalization in HF patients, despite female patients having been shown to have better self-care than males [16].

In the present study, we thus aimed to examine gender differences in status and prognostic associations of ScB of HF patients with mortality and hospitalization with a reference to ScB dimensions, using the database of the Chronic Heart Failure Analysis and Registry in the Tohoku District-2 (CHART-2) Study [17–19]. To assess ScB in HF patients, we employed the European Heart Failure Self-Care Behaviour Scale (EHFScBS) [14,15] in the present study.

Methods

The CHART-2 Study

The CHART-2 Study is a prospective multicenter observational study, as previously described (NCT00418041) [17–19]. Briefly, a total of 10,219 consecutive patients older than 20 years with coronary artery disease (Stage A), those at high risk for heart failure (HF) (Stage B), and those with a previous or current history of HF (Stage C/D) were enrolled between October 2006 and March 2010 at Tohoku University Hospital and 23 affiliated hospitals in the Tohoku District in Japan [17–19]. The diagnosis of HF was made by attending cardiologists based on the criteria of the Framingham Study [20] and the Stages of HF (A to D) was defined according to the American College of Cardiology Foundation (ACCF)/American Heart Association (AHA) guidelines [3]. The investigation conforms with the principles outlined in the

Declaration of Helsinki [21]. The present study was approved by the local ethics committee in each participating hospital and written informed consent was given by all patients [17–19].

The European Heart Failure Self-Care Behaviour Scale

EHFScBS was developed and published in 2003 to measure the behaviors that HF patients perform to maintain life, healthy functioning, and well-being (eTable 1) [14]. Conceptually, EHFScBS has 3 dimensions consisting of a total 12 items with a 5-point scale between 1 (I completely agree) and 5 (I completely disagree). The total score ranges from 12 to 60, and the higher the score is, the lower the ScB is. The first dimension ('complying with regimen') covers 6 items related to daily weighing, fluid and sodium restriction, medication, preventing influenza, and exercising. The second dimension ('asking for help') covers 4 items related to seeking help in case of weight gain, dyspnea, edema, and fatigue. The third dimension ('adapting activities') contains 2 items related to adapting one's activities to the condition. EHFScBS is available in 14 languages [22,23] and the validity and reliability of EHFScBS have been confirmed in a previous study in Japan [8].

Data collection flow

Among patients registered in the CHART-2 Study, we sent the questionnaire including EHFScBS to 8153 patients (79.8%) who were alive in September 2012. By the end of 2012, we received a reply from 5177 patients (63.5%). After excluding 134 patients who did not answer to more than 3 items of EHFScBS and 2810 Stage A/B patients, we finally collected ScB data in 2233 consecutive patients with Stage C/D HF (Fig. 1). In the present study, score 3 was given to the missing item [14,15]. The frequency of missing data varied between 0.2 and 1.9% across the items in EHFScBS.

Assessment of prognostic relevance of ScB

We examined the relationship between EHFScBS and prognostic outcomes, defined as all-cause death and hospitalization for HF. The follow-up period was between September 2012 and March 2015. Median values were used to split patients by their ScB [12]; by the median score 33, patients were categorized into high (score

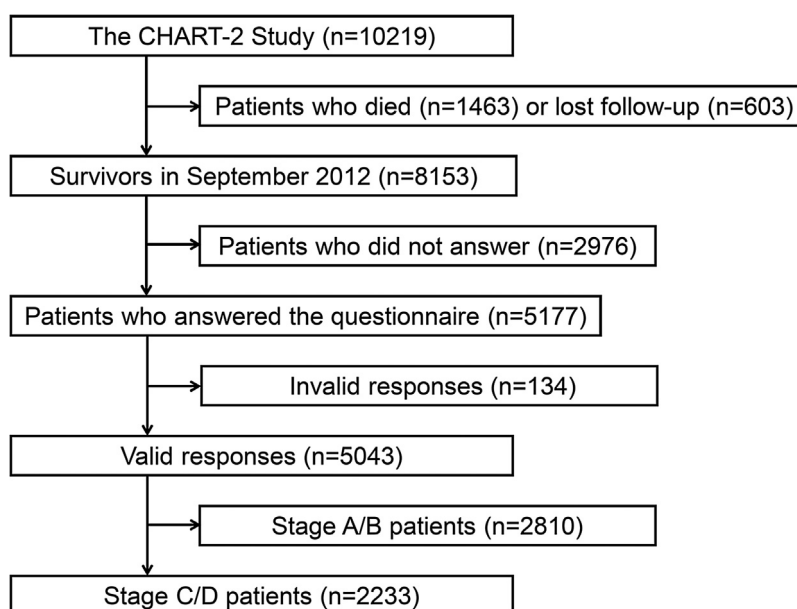


Fig. 1. Study flow diagram. The CHART-2 Study, The Chronic Heart Failure Analysis and Registry in the Tohoku District-2 Study

12–32, $n = 1090$) and low ScB (score 33–60, $n = 1143$) for global EHfScBS, while scores 6–15, 4–11, and 2–4 were used to define high ScB for each EHfScBS dimension, namely, complying with regimen, asking for help, and adapting activities, respectively. We defined high performance of each EHfScBS item by scores ≤ 2 [24].

Statistical analysis

Continuous variables were shown as mean \pm standard deviation (SD). For the cases of skewed distributions, median with interquartile range (IQR) was used instead of mean \pm SD. All categorical variables were presented as frequency (percentage). Gender differences in the observed values were compared by Welch's *t*-test for continuous variables and Fisher's exact test for categorical variables. Kaplan–Meier curves were utilized to estimate the incidence rates of all-cause death or hospitalization for HF, and the differences between high and low ScB groups were compared by the log-rank test. We constructed multiple Cox proportional hazards regression models to examine the effects of ScB on mortality and hospitalization, with stepwise variable selection using the following covariates, which were selected based on the previous literature: age, gender, systolic blood pressure (BP), diastolic BP, heart rate, body mass index (BMI), smoking status (never vs. current or past smoker), history of hospitalization for HF, hypertension, diabetes mellitus, atrial fibrillation, cerebrovascular disease, cancer, blood chemistry data [serum levels of hemoglobin, albumin, brain natriuretic peptide (BNP) and estimated glomerular filtration rate (eGFR)], left ventricular ejection fraction (LVEF), HF etiologies [ischemic heart disease, dilated cardiomyopathy, hypertrophic cardiomyopathy, valvular heart disease, and hypertensive heart disease] and medical treatment [β -blockers, calcium channel blockers, renin-angiotensin system inhibitors, diuretics, and statins] [17–19]. To adjust confounding effects and differences in the patient background, the inverse probability of treatment weighted (IPTW) using propensity score (PS) was also used [25]. For calculation of PS, we used a logistic regression model to regress for the following baseline characteristics: age, systolic BP, diastolic BP, heart rate, BMI, smoking status, history of hospitalization for HF, hypertension, diabetes mellitus, atrial fibrillation, cerebrovascular disease, myocardial infarction, cancer, hemoglobin, albumin, BNP, eGFR, LVEF, β -blockers, calcium channel blockers, renin-angiotensin system inhibitors, diuretics, and statins. Logistic regression analysis with stepwise variable selection was used to assess factors associated with high and low ScB, using the same covariates as those used in the Cox proportional hazards models. The item analysis was performed by calculating the distribution of the high performance of each self-care behavior. The item total correlation of the items and Cronbach's alpha if the item was deleted were calculated. All statistical analyses were performed using R statistical software (version 3.3.1) (R Foundation for Statistical Computing, Vienna, Austria) [26]. A *p*-value < 0.05 was considered to be statistically significant.

Results

Patient characteristics and factors associated with ScB

The patient characteristics at baseline are shown in Table 1. Mean age was 71.8 ± 11.0 years and female patients accounted for 29.1% of the subjects. Mean LVEF was $57.1 \pm 15.1\%$. The prevalence of prior hospitalization for HF was 54.3%. Male patients ($n = 1583$), as compared with females ($n = 650$), were characterized by younger age, lower LVEF, less advanced New York Heart Association class, lower BNP level, and higher prevalence of ischemic heart disease. eTable 2 shows a comparison of baseline characteristics between low and high ScB patients in both genders.

The simple logistic regression analysis showed that female gender was significantly associated with high ScB [odds ratio 1.27, 95% confidence interval (CI) 1.01 to 1.58, $p = 0.045$] (eTable 3).

Item analysis

As shown in eFigure 1, female patients had lower EHfScBS score in total (median 33 vs. 31, $p < 0.001$) as well as in all 3 dimensions consisting of complying with regimen, asking for help, and adapting activities. As shown in eTable 4, Cronbach's alpha was 0.77 and the most frequently performed self-care behavior items were taking medications as prescribed (item 10), patients do not necessarily weigh themselves (item 1), limit drinking fluids or taking salts (items 6 and 9), and exercise regularly (item 12). In addition, patients do not necessarily contact their doctors or nurses even if they feel changes in their bodies or symptoms (items 2, 3, 4, 5, and 8).

Prognostic relevance of ScB with mortality and HF hospitalization

During the median follow-up period of 2.57 years, all-cause death occurred in 268 patients (12.0%) and hospitalization for HF in 267 (12.0%). In the overall population without considering gender, high global ScB was associated with neither all-cause death nor hospitalization for HF even after adjustment with clinical backgrounds [adjusted hazard ratio (aHR) 1.20, 95% CI 0.92 to 1.58, $p = 0.177$, and aHR 1.04, 95% CI 0.80 to 1.36, $p = 0.773$, respectively]. Kaplan–Meier curves showed that the patients with high global ScB had significantly higher occurrence of the all-cause death and hospitalization for HF in the entire cohort, particularly in males but not in females (Fig. 2). After adjustment with clinical backgrounds in the multiple Cox proportional hazards models with stepwise selection, high global ScB patients, as compared with low global ScB patients, had significantly increased risk for all-cause death in males, but not in females, with a significant gender difference (p for interaction 0.020) (Fig. 3). Moreover, IPTW using PS also showed that high ScB patients, as compared with low ScB patients, had significantly increased risk for all-cause death in males (aHR 1.29, 95% CI 1.04 to 1.60, $p = 0.020$) but not in females (aHR 0.84, 95% CI 0.57 to 1.23, $p = 0.366$). Furthermore, among the 3 dimensions in EHfScBS, complying with regimen was associated with decreased mortality in females, but not in males (p for interaction 0.003), while asking for help was related with increased incidence of HF hospitalization than low ScB in males but not in females (p for interaction 0.048). Adapting activities was associated with increased mortality and tended to be associated with increased incidence of HF hospitalization comparably in both genders.

Prognostic relevance of self-care behavior items with mortality and HF hospitalization

Table 2 shows the results of the multiple Cox proportional hazards models for all-cause death and HF hospitalization in each EHfScBS item. After adjustment with clinical backgrounds, taking rest if shortness of breath occurs, asking help for leg edema, and fluid restriction and resting during the day were significantly associated with an increased risk for mortality, while high self-reported exercise was associated with a decreased risk for mortality (aHR: 0.62; 95% CI: 0.44 to 0.86; $p = 0.004$). Fig. 4 shows the results of the multiple Cox proportional hazards models for all-cause death and HF hospitalization in each EHfScBS item by gender. The analysis of interactions showed significant gender differences in the impact on all-cause death of daily weighing and asking help for shortness of breath, and that on HF hospitalization of asking help for shortness of breath and leg edema, resting during the day, and sodium restriction. Importantly, among the items of

Table 1
Baseline characteristics of patients.

	All patients (n = 2233)	Gender differences		p-Value
		Male (n = 1583)	Female (n = 650)	
Age (years)	71.8 ± 11.0	71.1 ± 10.8	73.4 ± 11.5	<0.001
BMI (kg/m ²)	24.1 ± 3.6	23.8 ± 3.4	24.1 ± 3.8	0.027
Systolic BP (mmHg)	125.8 ± 18.1	126.2 ± 17.6	125.0 ± 19.2	0.156
Diastolic BP (mmHg)	73.1 ± 11.3	73.7 ± 11.2	71.5 ± 11.5	<0.001
Heart rate (beat/min)	71.4 ± 14.4	70.6 ± 14.0	73.2 ± 15.4	<0.001
NYHA class III–IV, n (%)	142 (6.4)	74 (4.7)	68 (10.5)	<0.001
Current or past smoker, n (%)	995 (47.0)	919 (61.3)	76 (12.4)	<0.001
Previous history, n (%)				
Hospitalization for HF	1213 (54.3)	839 (53.0)	374 (57.5)	0.056
Hypertension	1927 (86.3)	1388 (87.7)	539 (82.9)	0.004
Diabetes mellitus	851 (38.1)	635 (40.1)	216 (33.2)	0.003
Dyslipidemia	1847 (82.7)	1328 (83.9)	519 (79.8)	0.025
Atrial fibrillation	799 (35.8)	555 (35.1)	244 (37.5)	0.293
Stroke	346 (15.5)	251 (15.9)	95 (14.6)	0.502
Cancer	249 (11.2)	172 (10.9)	77 (11.8)	0.552
Etiology of HF, n (%)				
IHD	1142 (51.1)	908 (57.4)	234 (36.0)	<0.001
VHD	178 (8.0)	82 (5.2)	96 (14.8)	<0.001
DCM	319 (14.3)	243 (15.4)	76 (11.7)	0.029
HCM	72 (3.2)	46 (2.9)	26 (4.0)	0.231
HHD	396 (17.7)	249 (15.7)	147 (22.6)	<0.001
Laboratory findings				
Hemoglobin (g/dl)	13.5 ± 1.8	13.9 ± 1.8	12.5 ± 1.5	<0.001
BUN (mg/dl)	18.2 ± 7.2	18.2 ± 7.0	18.1 ± 7.8	0.812
Creatinine (mg/dl)	1.0 ± 0.6	1.0 ± 0.6	0.8 ± 0.6	<0.001
Albumin (g/dl)	4.2 ± 0.4	4.2 ± 0.4	4.1 ± 0.5	0.057
LDL-C (mg/dl)	105.3 ± 30.5	104 ± 29.8	108.5 ± 31.9	0.008
HDL-C (mg/dl)	51.5 ± 14.7	49.8 ± 14.4	55.7 ± 14.6	<0.001
Triglyceride (mg/dl)	135.8 ± 94.5	140.7 ± 102.3	123.6 ± 70.2	<0.001
HbA1c (%)	6.3 ± 0.9	6.3 ± 0.9	6.3 ± 0.9	0.528
eGFR (ml/min/1.73 m ²)	63.6 ± 19.5	64.2 ± 19.0	62.2 ± 20.6	0.032
BNP (pg/ml)	79.2 (32.9, 189.0)	71.5 (29.1, 175.0)	98.2 (42.8, 216.0)	<0.001
Echocardiography				
LVEF (%)	57.1 ± 15.1	55.6 ± 14.8	60.7 ± 15.2	<0.001
Medications, n (%)				
Diuretics	1119 (50.1)	747 (47.2)	372 (57.2)	<0.001
RAS inhibitors	1609 (72.1)	1180 (74.5)	429 (66.0)	<0.001
β-blockers	1156 (51.8)	850 (53.7)	306 (47.1)	0.005
CCB	891 (39.9)	635 (40.1)	256 (39.4)	0.786
Statins	971 (43.5)	711 (44.9)	260 (40.0)	0.037
Digitalis	479 (21.5)	308 (19.5)	171 (26.3)	<0.001

Results are expressed as mean ± standard deviation for continuous variables. BMI, body mass index; BNP, brain natriuretic peptide; BUN, blood urea nitrogen; BP, blood pressure; CCB, calcium channel blockers; DCM, dilated cardiomyopathy; eGFR, estimated glomerular filtration rate; HbA1c, hemoglobin A1c; HCM, hypertrophic cardiomyopathy; HDL-C, high density lipoprotein cholesterol; HF, heart failure; HHD, hypertensive heart disease; IHD, ischemic heart disease; LDL-C, low density lipoprotein cholesterol; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; RAS, renin-angiotensin system; VHD, valvular heart disease.

complying with regimen, ScB for daily weight monitoring was associated with decreased mortality in females, but not in males, while ScB for regular exercise was associated with decreased mortality comparably in both genders. As for HF hospitalization, ScB for sodium restriction was associated with increased incidence in males, but not in females. Among the items of asking for help, seeking help for dyspnea and edema was significantly associated with increased incidence of all-cause death and hospitalization for HF in males but not in females.

Discussion

The present study clearly demonstrated gender differences in prognostic relevance of ScB as follows: (1) patients with high global ScB, as compared with those with low global ScB, had significantly increased all-cause mortality in males but not in females, and (2) among the 3 dimensions in EHFScBS, high ScB for

complying with regimen was associated with decreased mortality in females, and high ScB for asking for help was associated with increased incidence of HF hospitalization in males, while high ScB for adapting activities was comparably associated with mortality in both genders.

This is one of the first reports to examine the prognostic relevance of global ScB in patients with HF. The results showed that high ScB was not necessarily associated with prognosis in our overall study population without considering gender. This observation was consistent with a recent report by Kessing et al. in which global self-care assessed with EHFScB-9 was not associated with long-term mortality in HF patients [12]. However, the present study provided further insights by examining associations between ScB and prognosis with reference to gender and 3 dimensions of EHFScBS. The present study clearly demonstrated that high global ScB was significantly associated with increased mortality in males and was not associated with

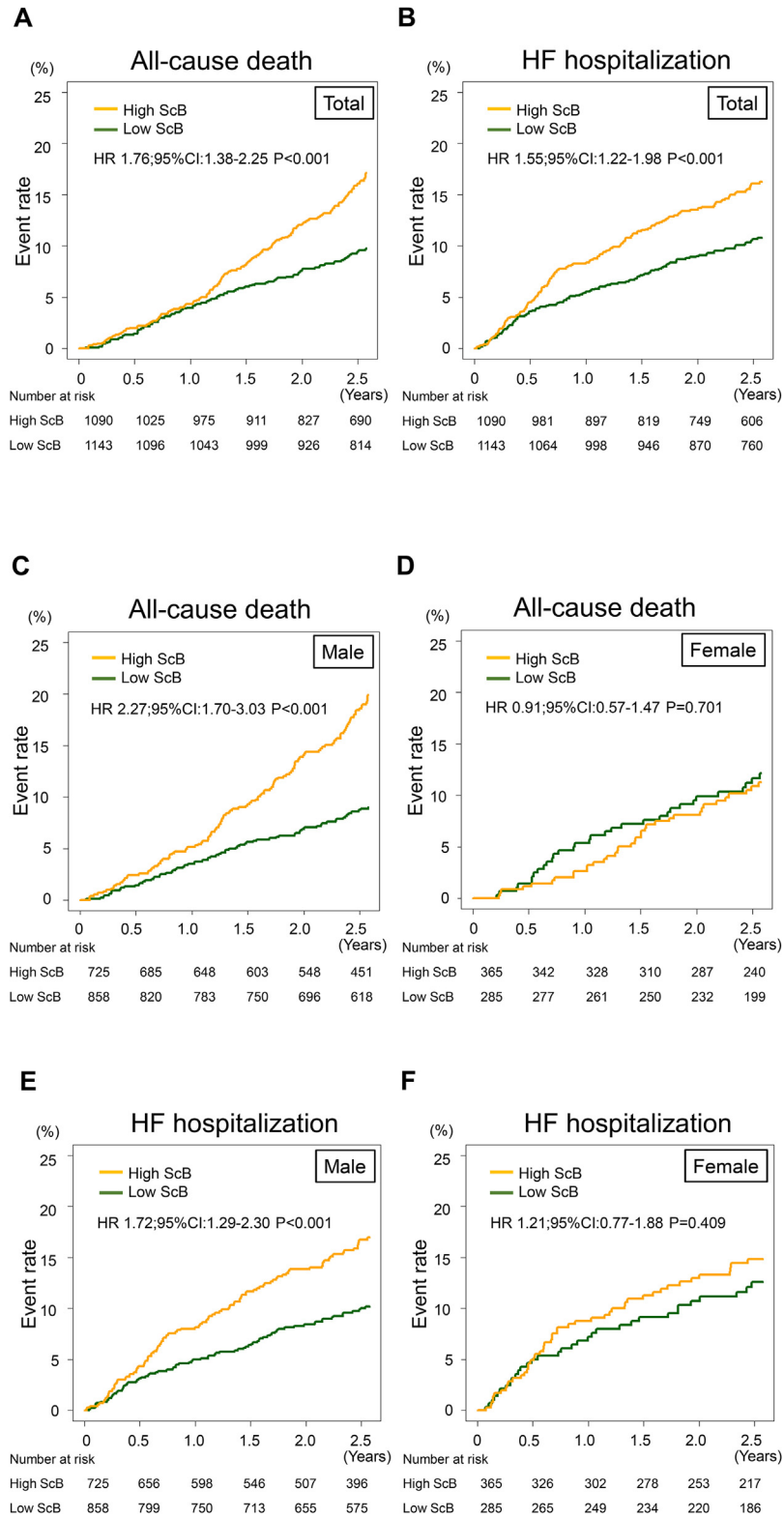


Fig. 2. Kaplan–Meier curves for prognosis. Kaplan Meier curves for (A, C, D) all-cause death and (B, E, F) heart failure admission (HF) in (A, B) total study group, (C, E) male, and (D, F) female patients. CI, confidence interval; HF, heart failure; HR, hazard ratio; ScB, self-care behaviors.

prognosis in females, even after adjustment of clinical backgrounds. Although the precise mechanisms for these unexpected findings are unclear, the following explanations are considered. First, as a nature of observational studies, it was difficult to show the cause-effect relationship between ScB and outcomes. Thus, these observations might represent a fact that patients with more severe HF were obliged to have both better ScB with consequent

worse prognosis in the present study. Second, there might be a limitation for the assessment of ScB using EHfScBS in the clinical settings, since EHfScBS does not include evaluation of prognostic factors, such as comorbidities including atrial fibrillation, diabetes, hypertension, anemia, iron deficiency, renal disease, arthritis, frailty, depression, and thyroid abnormalities, which female patients tend to have more frequently [27], and other factors

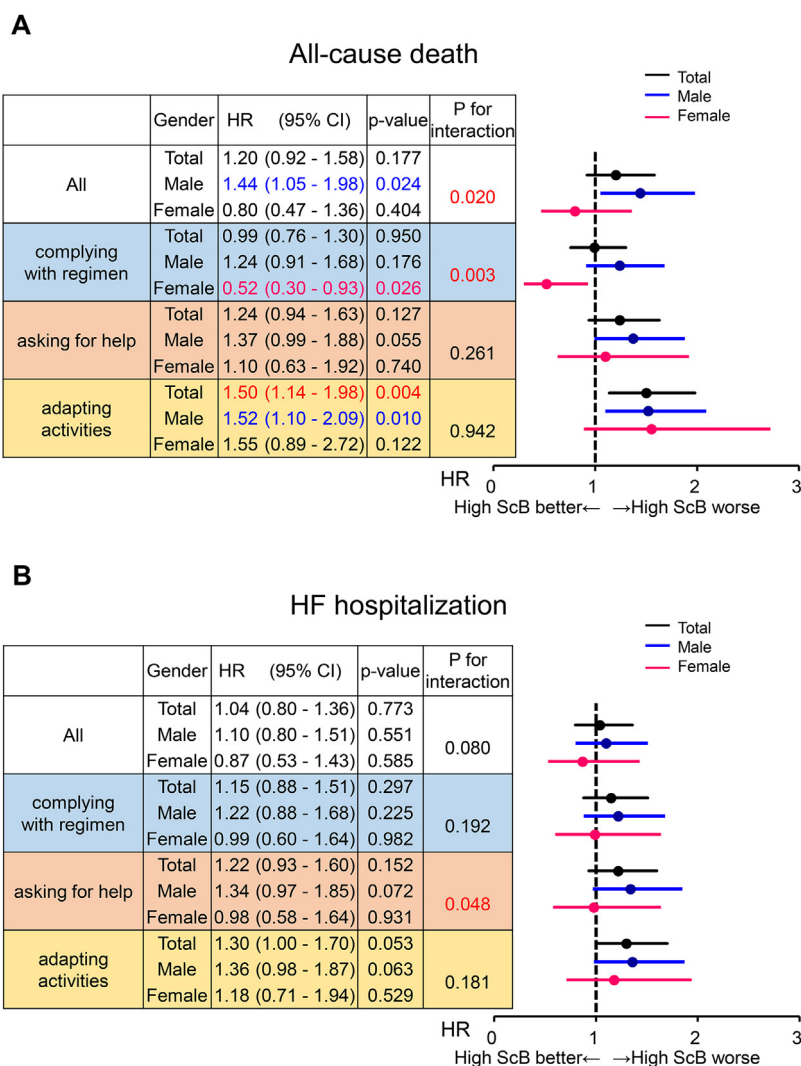


Fig. 3. Multiple analysis for all-cause death and heart failure hospitalization based on factor analysis. Forest plots for (A) all-cause death and (B) heart failure (HF) hospitalization. Following variables were selected in a stepwise fashion and used in the multiple Cox proportional hazards models; age, history of hospitalization for HF, diabetes mellitus, atrial fibrillation, cancer, serum levels of hemoglobin, brain natriuretic peptide (BNP), left ventricular ejection fraction (LVEF), and statins in mortality; age, blood pressure, heart rate, history of hospitalization for HF, diabetes mellitus, cerebrovascular disease, BNP, estimated glomerular filtration rate, LVEF, dilated cardiomyopathy, hypertrophic cardiomyopathy, β -blockers and diuretics in HF hospitalization. CI, confidence interval; HF, heart failure; HR, hazard ratio; ScB, self-care behaviors.

including living status (e.g. living alone and eating habits) by which male patients are often troubled [28]. Furthermore, although it has been reported that female patients had better self-care than males [16], gender differences might exist in quality of ScB, raising a concern that male patients, as compared with females, may not perform ScB in better quality to prevent worsening HF even though high ScB scores are given by EHfScBS.

The present study further demonstrated gender differences in prognostic relevance of ScB with reference to ScB dimensions. Among the 3 dimensions in EHfScBS, high ScB for complying with regimen was associated with decreased mortality in females, but not in males and high ScB for asking for help was associated with increased incidence of HF hospitalization in males, but not in females. In contrast, high ScB for adapting activities was comparably associated with mortality between both genders. These results are of clinical significance, warranting a need to be aware of gender differences in ScB and its prognostic impacts in the daily management of HF patients.

The present study underlined the importance of assessing ScB. In particular, monitoring of adherence and symptoms were important, since complying with the regimen in females and asking for help in males were related to the prognosis. Among the

items related to complying with the regimen, daily weighing was the only item showing gender differences for the impact on both all-cause death and HF hospitalization, while sodium restriction and influenza vaccination showed gender differences only for HF hospitalization and other items showed no gender differences. Considering the lack of differences in clinical background between patients with high and low ScB in females, this observation is important since this may indicate the benefit of ScB without an influence of reverse-causality. It was also noted that daily exercise was associated with improved mortality in HF patients without interaction with gender. Among the items of ScB, ScB for exercise has been most frequently examined and shown to be associated with improved outcomes [13,29]. Thus, physical activity could be an important therapeutic target to improve the long-term prognosis of chronic HF patients, although exercise should be introduced carefully considering that physical symptoms (27%) and a lack of energy (25%) could be the reasons for inactivity in HF patients [30]. Indeed, a meta-analysis showed that cardiac rehabilitation reduced mortality and hospitalizations [29] and it was reported that 80% of patients recognized importance to engage in some exercise, although only 39% of them reported doing so [30]. Further studies are needed to examine the correspondence

Table 2
Multiple analysis for all-cause death and heart failure hospitalization.

EHFScBS		All-cause death			HF hospitalization		
		HR	95% CI	p-Value	HR	95% CI	p-Value
1	I weigh myself every day	0.86	0.65–1.14	0.280	0.99	0.76–1.31	0.968
2	If I get short of breath, I take it easy	1.38	1.05–1.81	0.022	1.29	0.99–1.69	0.060
3	If my shortness of breath increases, I contact my doctor or nurse	1.19	0.91–1.55	0.211	1.20	0.92–1.56	0.178
4	If my feet/legs become more swollen than usual, I contact my doctor or nurse	1.33	1.01–1.74	0.040	1.37	1.05–1.78	0.020
5	If I gain 2 kg in 1 week, I contact my doctor or nurse	1.21	0.92–1.59	0.163	0.95	0.72–1.25	0.707
6	I limit the amount of fluids I drink (not more than 1.5–2 l/day)	1.35	1.00–1.83	0.049	1.19	0.88–1.63	0.262
7	I take a rest during the day	1.81	1.33–2.47	<0.001	1.34	1.01–1.79	0.044
8	If I experience increased fatigue, I contact my doctor or nurse	1.22	0.93–1.59	0.152	1.13	0.86–1.47	0.384
9	I eat a low salt diet	1.23	0.95–1.60	0.116	1.29	0.99–1.68	0.055
10	I take my medication as prescribed	0.67	0.38–1.18	0.166	1.54	0.68–3.48	0.299
11	I get a flu shot every year	1.04	0.79–1.38	0.787	1.08	0.81–1.42	0.608
12	I exercise regularly	0.62	0.44–0.86	0.004	0.76	0.55–1.04	0.087

Multiple analysis for all-cause death and heart failure hospitalization CI, confidence interval; EHFScBS, European Heart Failure Self-Care Behaviour Scale; HF, heart failure; HR, hazard ratio. The following variables were selected in a stepwise fashion and used in the multiple Cox proportional hazards models: age, history of hospitalization for HF, diabetes mellitus, atrial fibrillation, cancer, serum levels of hemoglobin, brain natriuretic peptide (BNP), left ventricular ejection fraction (LVEF), and statins in mortality; age, blood pressure, heart rate, history of hospitalization for HF, diabetes mellitus, cerebrovascular disease, BNP, estimated glomerular filtration rate, LVEF, dilated cardiomyopathy, hypertrophic cardiomyopathy, β -blockers, and diuretics in HF hospitalization.

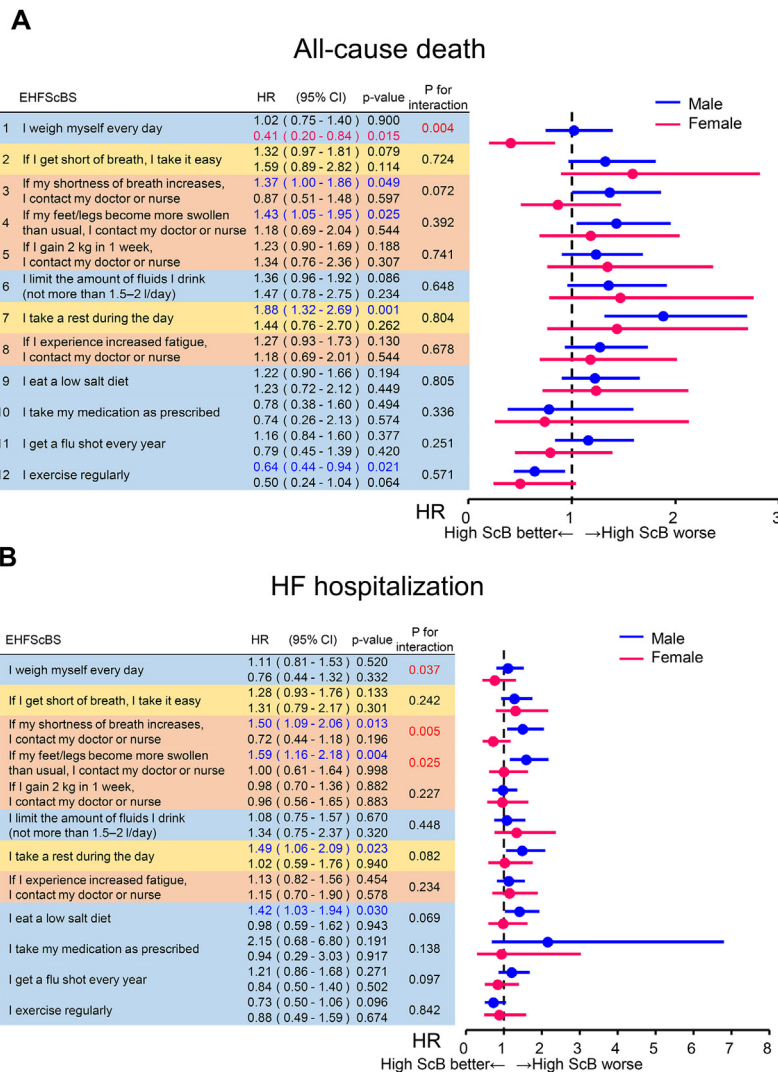


Fig. 4. Multiple analysis for all-cause death and heart failure hospitalization based on item analysis. Forest plots for (A) all-cause death and (B) heart failure (HF) hospitalization.

The following variables were selected in a stepwise fashion and used in the multiple Cox proportional hazards models: age, history of hospitalization for HF, diabetes mellitus, atrial fibrillation, cancer, serum levels of hemoglobin, brain natriuretic peptide (BNP), left ventricular ejection fraction (LVEF) and statins in mortality; age, blood pressure, heart rate, history of hospitalization for HF, diabetes mellitus, cerebrovascular disease, BNP, estimated glomerular filtration rate, LVEF, dilated cardiomyopathy, hypertrophic cardiomyopathy, β -blockers, and diuretics in HF hospitalization. CI, confidence interval; EHFScBS, European Heart Failure Self-Care Behaviour Scale; HF, heart failure; HR, hazard ratio; ScB, self-care behaviors.

between subjectively and objectively measured self-care, such as exercising regularly and daily weighing, and its actual relationship with long-term prognosis. We also observed gender differences in the prognostic relevance of ScB related to asking for help. As compared with females, ScB for asking for help and increase in shortness of breath and leg edema was significantly associated with increased incidence of death and/or HF hospitalization in males, indicating an importance to listen to clinical complaints of male HF patients more carefully than those of females. Importantly, since male patients have worse prognosis than female patients [18], we should pay more attention to clinical complaints, particularly in male patients with HF to improve clinical outcomes.

Limitations

Several limitations should be mentioned for the present study. First, since our CHART-2 Study is an observational study in Japan, caution should be taken when generalizing the present findings to other populations, although clinical characteristics and the results of item analysis were almost comparable to those reported in the previous study from Japan and other countries. Second, considering the nature of an observational study, the observed relationships between ScB and prognosis should be interpreted carefully considering a possibility of reverse-causality. Third, the collection rate of valid responses to the questionnaire was relatively low (5177/8153 patients, 63.5%), raising a possibility of selection bias of the study cohort. Fourth, self-reporting tends to overestimate the patient's true adherence [31], which might have affected the present results. Fifth, since the sample size in this study was relatively big, some of the statistically significant results could be incidental. Sixth, since we transformed ordinal EHfScBS into a categorical variable, we may have missed some important information. Finally, we did not consider several factors making self-care difficult including depression, cognitive function [32], and living status [28] as confounding factors in this study. Thus, further investigations are warranted to confirm our present observations.

Conclusions

This study is the first that demonstrates gender differences in prognostic relevance in ScB with special reference to gender and self-care dimensions. Randomized clinical trials of patients with HF, in which subjective and objective measures of self-care are assessed during the follow-up, would provide further insight into the long-term effects of self-care on prognosis. Furthermore, it is necessary to establish a system (visit, telephone, internet, etc.), since HF programs enable clinicians and researchers to help patients learn effective self-care strategies using other methods, such as written or verbal education, and change their behaviors, as well as to detect exacerbation of HF in its early stage and reduce HF hospitalization, cardiac events, and/or all-cause deaths [8].

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Conflicts of interest

The authors declare that there is no conflict of interest.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jjcc.2018.11.006.

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