ESC HEART FAILURE
ESC Heart Failure 2020; **7**: 2485–2493
Published online 24 July 2020 in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/ehf2.12815

ORIGINAL RESEARCH ARTICLE

Sex differences in patients with acute decompensated heart failure in Japan: observation from the KCHF registry

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Abstract

Aims The association between sex and long-term outcome in patients hospitalized for acute decompensated heart failure (ADHF) has not been fully studied yet in Japanese population. The aim of this study was to determine differences in baseline characteristics and management of patients with ADHF between women and men and to compare 1-year outcomes between the sexes in a large-scale database representing the current real-world clinical practice in Japan.

Methods and results Kyoto Congestive Heart Failure registry is a prospective cohort study enrolling consecutive patients hospitalized for ADHF in Japan among 19 centres. Baseline characteristics, clinical presentation, management, and 1-year outcomes were compared between men and women. A total of 3728 patients who were alive at discharge constituted the current study population. There were 1671 women (44.8%) and 2057 men. Women were older than men [median (IQR): 83 (76–88) years vs. 77 (68–84) years, $P < 0.0001$]. Hypertensive and valvular heart diseases were more prevalent in women than in men (28.0% vs. 22.5%, $P = 0.0001$; and 26.9% vs. 14.0%, $P < 0.0001$, respectively), whereas ischaemic aetiology was less prevalent in women than in men (20.0% vs. 32.5%, $P < 0.0001$). Women less often had reduced left ventricular ejection fraction (<40%) than men (27.5% vs. 45.1%, $P < 0.0001$). The cumulative incidence of all-cause death or hospitalization for heart failure was not significantly different between women and men (33.6% vs. 34.3%, $P = 0.71$), although women were substantially older than men. After multivariable adjustment, the risk of all-cause death or hospitalization for heart failure was significantly lower among women (adjusted hazard ratio: 0.84, 95% confidence interval: 0.74–0.96, $P = 0.01$).

Conclusions Women with heart failure were older and more often presented with preserved EF with a non-ischaemic aetiology and were associated with a reduced adjusted risk of 1-year mortality compared with men in the Japanese population.

Keywords Heart failure; Sex difference; Prognosis

Received: 20 February 2020; Revised: 11 May 2020; Accepted: 20 May 2020
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Introduction

Several aspects of sex-related differences in heart failure (HF) were well known. Previous studies have reported that HF with preserved ejection fraction is more frequent in women than in men,[1–4] and the average age of patients with HF is older in women than in men.[5,6] Furthermore, women are associated with a lower risk for mortality due to HF in general.[3,7–11] However, these studies were conducted from the 1990s to the early 2000s. The population, especially in Japan, has been ageing rapidly, and the proportion of population over 65 years of age had already reached 25% in 2013. The demographics and outcomes of HF patients continue changing, and the current trend in clinical practice needs to be clarified. Therefore, the aim of this study was to determine differences in baseline characteristics and management of patients with acute decompensated HF (ADHF) between women and men and to compare 1-year outcomes between the sexes in a large-scale database representing the current real-world clinical practice in Japan.

Methods

Study population

The Kyoto Congestive Heart Failure (KCHF) registry is a physician-initiated, prospective, multicentre cohort study enrolling consecutive patients who were hospitalized and underwent HF-specific treatment involving intravenous drugs within 24 h after hospital presentation due to ADHF defined by the modified Framingham criteria for the first time between October 2014 and March 2016, in 19 secondary and tertiary hospitals, including rural/urban, and large/small hospitals, in Japan. Details of the KCHF registry have been described previously.[12] The study protocol was approved by the institutional review board of each participating centre. Patient records were anonymized prior to analysis. A waiver of written informed consent from each patient was approved because it met the following conditions in accordance with Japan's ethics guidelines for epidemiologic research[13] and Policy for Protection of Human Research Subjects in the United States[14]: (i) we would use clinical information obtained in routine practice on the medical record without any risk to the subjects; (ii) the waiver of normal consent procedures would not adversely affect the rights and welfare of the subjects; (iii) the research could not be carried out effectively without the waiver; and (iv) the subjects were provided with additional pertinent information and had the right to opt out of this study whenever appropriate.[15]

Detailed definitions of baseline clinical characteristics, including the signs and symptoms of HF, were described previously.[16] Clinical follow-up data were collected in October 2017. The attending physicians or research assistants at each participating hospital collected data regarding clinical events after the index hospitalization from hospital charts or by contacting patients, their relatives, or their referring physicians with consent. The follow-up was censored at 1 year. The primary outcome measure was a composite of all-cause death or hospitalization due to HF at 1 year, and secondary outcome measures were all-cause deaths, cardiac death, and hospitalization for HF.

Statistical analysis

In the present analysis, we compared 1-year clinical outcomes between women and men.

Categorical variables were presented as counts with percentages and compared using the χ^2 test. Continuous variables were expressed as the mean with standard deviation or median with interquartile range and compared using the Student's *t*-test or the Wilcoxon rank-sum test, as appropriate.

To compare the 1-year clinical outcomes, the Kaplan–Meier method was used to estimate cumulative incidences of clinical event rates, and differences were assessed using the log-rank test. The date of discharge from the index hospitalization was regarded as time zero for clinical follow-up. We used a multivariable Cox proportional hazard model to estimate the hazard ratios and 95% CIs of the primary and secondary outcome measures in women relative to those in men. Proportional hazard assumptions were assessed on the plots of log (time) vs. log [−log (survival)] stratified by the variables and are verified to be acceptable. Consistent with the previous report[17] and two additional factors [pulmonary oedema (using of non-invasive positive-pressure ventilation or intubation at admission) and implantable cardioverter defibrillator (ICD) or cardiac resynchronization therapy (CRT) device implantation], we selected 25 clinically relevant risk-adjusting variables listed in *Table 1*.For the risk-adjusting variables, continuous variables were dichotomized by clinically meaningful reference values or median values: age $\geq$ 80 years based on the median value, left ventricular ejection fraction (LVEF) < 40% based on the HF guideline of LVEF classification,[18] body mass index <22 kg/m^2, renal dysfunction (estimated glomerular filtration rate < 30 mL/min/1.73m^2) based on the chronic kidney disease (CKD) grade, decreased albumin levels (serum level < 3.0 g/dL), and hyponatremia (serum sodium level < 135 mEq/L). We also conducted subgroup analyses stratified by age, aetiologies of HF including acute coronary syndrome, non-acute ischaemic aetiology, and non-ischaemic aetiology, LVEF, social backgrounds (ambulatory and living status), the presence of diabetes, and the troponin values dichotomized based on the median value. All statistical analyses were conducted by a physician (E. Y.) and a statistician (T. M.) using JMP 13.0 (SAS Institute Inc, Cary, NC). Two-tailed *P* values < 0.05 were considered statistically significant.

Table 1 Baseline characteristics (3728 patients with 1-year follow-up)

	Men (N = 2057)	Women (N = 1671)	P value
Demographics			
Age, years			
Median (IQR)	77 (68–84)	83 (76–88)	<0.0001
Mean	75 ± 12	81 ± 11	<0.0001
Age ≥ 80 years[a]	858 (41.7)	1075 (64.3)	<0.0001
BMI, kg/m^2	23.4 ± 4.3	22.2 ± 4.6	<0.0001
BMI <22 kg/m^2 [a]	777 (39.1)	862 (54.9)	<0.0001
Medical history			
Prior hospitalization due to HF[a]	718 (35.5)	603 (36.8)	0.42
Atrial fibrillation/flutter[a]	811 (39.4)	745 (44.6)	0.002
Hypertension[a]	1468 (71.4)	1231 (73.7)	0.12
Diabetes mellitus[a]	853 (41.5)	544 (32.6)	<0.0001
Dyslipidemia	878 (39.2)	671 (36.9)	0.13
Prior myocardial infarction[a]	562 (27.3)	276 (16.5)	<0.0001
Prior PCI/CABG	629 (30.6)	327 (19.6)	<0.0001
Prior device implantation			
Pacemaker	101 (4.9)	136 (8.1)	<0.0001
ICD[a]	42 (2.0)	17 (1.0)	0.012
CRTP/CRTD[a]	60 (2.9)	12 (0.7)	<0.0001
Current smoking[a]	382 (18.9)	71 (4.3)	<0.0001
Prior stroke[a]	342 (16.6)	251 (15.0)	0.18
Chronic kidney disease	974 (47.4)	670 (40.1)	<0.0001
Malignancy	339 (16.5)	198 (11.9)	<0.0001
Chronic lung disease[a]	326 (15.9)	163 (9.8)	<0.0001
Dementia	264 (12.8)	394 (23.6)	<0.0001
Medications prior to admission			
ACE-Is/ARBs	939 (45.7)	764 (45.7)	0.86
MRAs	343 (16.7)	310 (18.6)	0.47
Beta-blockers	825 (40.1)	645 (38.6)	0.58
Tolvaptan	113 (5.1)	57 (3.1)	0.003
Social backgrounds			
Poor medical adherence	362 (17.6)	267 (16.0)	0.19
Life style			<0.0001
Living alone[a]	417 (20.9)	379 (23.4)	
With a partner only	698 (35.0)	258 (16.0)	
With family members	801 (40.2)	822 (50.8)	
Institution for aged or hospital	76 (3.8)	158 (9.8)	
Daily life activities			<0.0001
Ambulatory[a]	1742 (85.4)	1207 (73.1)	
Use of wheelchair [outdoor only]	108 (5.3)	167 (10.1)	
Use of wheelchair [outdoor and indoor]	136 (6.7)	201 (12.2)	
Bedridden	53 (2.6)	76 (4.6)	
Aetiology			<0.0001
Acute coronary syndromes[a]	134 (6.5)	72 (4.3)	
Ischaemic (non-acute)	669 (32.5)	334 (20.0)	
Hypertensive heart disease	462 (22.5)	467 (28.0)	
Cardiomyopathy	359 (17.5)	198 (11.6)	
Valvular heart disease	288 (14.0)	449 (26.9)	
Aortic stenosis	90 (4.4)	169 (10.1)	
Mitral regurgitation	102 (5.0)	133 (8.0)	
Presentation on admission			
LVEF, %	41 (31–56)	52 (38–63)	<0.0001
HFrEF (LVEF < 40%)[a]	925 (45.1)	458 (27.5)	<0.0001
sBP < 90mmHg[a]	59 (2.9)	36 (2.2)	0.17
HR < 60 bpm[a]	133 (6.5)	119 (7.2)	0.42
Atrial fibrillation/flutter	710 (34.5)	647 (38.7)	0.008
NYHA III/IV	1778 (86.6)	1453 (87.6)	0.38
Pulmonary oedema[a]	340 (16.5)	237 (14.2)	0.049
Laboratory data on admission			
Hb, mg/dL	12.1 (10.3–13.8)	10.9 (9.6–12.3)	<0.0001
Anaemia [a, b]	1293 (63.0)	1169 (70.0)	<0.0001
BNP	721 (402–1265)	704 (385–1258)	0.72
eGFR, mL/min	45 (30–61)	42 (27–59)	0.01
eGFR < 30 mL/min[a]	567 (25.4)	551 (30.4)	0.0004
Sodium, mEq/L	139 (137–142)	140 (137–142)	0.002

(*Continues*)

Table 1 (continued)

	Men (*N* = 2057)	Women (*N* = 1671)	*P* value
Sodium < 135 mEq/L[a]	243 (11.9)	191 (11.5)	0.72
Albumin, mg/dL	3.5 (3.2–3.8)	3.5 (3.2–3.8)	0.17
Albumin < 3.0 mg/dL[a]	269 (13.5)	213 (13.2)	0.81
Management after admission			
Respiratory management			0.0008
None	566 (27.5)	449 (26.9)	
Oxygen inhalation	1151 (56.0)	985 (59.0)	
NPPV	288 (14.0)	223 (13.4)	
Intubation	52 (2.5)	14 (0.8)	
Inotropes	80 (3.9)	47 (2.8)	0.04
LV support device			
IABP	56 (2.7)	29 (1.7)	0.04
PCPS	6 (0.3)	1 (0.1)	0.10
Procedural interventions			
Coronary angiography	795 (38.7)	418 (25.0)	<0.0001
PCI	241 (11.7)	117 (7.0)	<0.0001
CABG	3 (0.2)	0	0.12
Pacemaker implantation	33 (1.6)	33 (2.0)	0.39
ICD implantation[a]	9 (0.4)	3 (0.2)	0.17
CRTP/CRTD implantation[a]	16 (0.8)	5 (0.3)	0.052
Medication at discharge			
ACE-Is/ARBs[a]	1248 (60.7)	894 (53.5)	<0.0001
MRAs[a]	915 (44.5)	765 (45.8)	0.43
Beta-blockers[a]	1444 (70.2)	1029 (61.6)	<0.0001
Tolvaptan	237 (11.5)	155 (9.3)	0.03

BMI, body mass index; HF, heart failure; PCI, percutaneous coronary interventions; CABG, coronary artery bypass graft; ICD, implantable cardioverter defibrillator; CRTP, cardiac resynchronization therapy pacemaker; CRTD, cardiac resynchronization therapy defibrillator; ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; MRA, mineralocorticoid receptor antagonist; HFrEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; BNP, brain-type natriuretic peptide; eGFR, estimated glomerular filtration rate; NPPV, noninvasive positive-pressure ventilation; IABP, intra-aortic balloon pump; PCPS, percutaneous cardiopulmonary support

[a]Risk adjusting variables selected for Cox proportional hazard models.

[b]Defined by the World Health Organization criteria (haemoglobin <12 g/dL for women and <13 g/dL for men).

[c]Pulmonary oedema was defined as using of NPPV or intubation at admission. Previous and current ICD and CRTP/CRTD implantation were treated as one variable.

Results

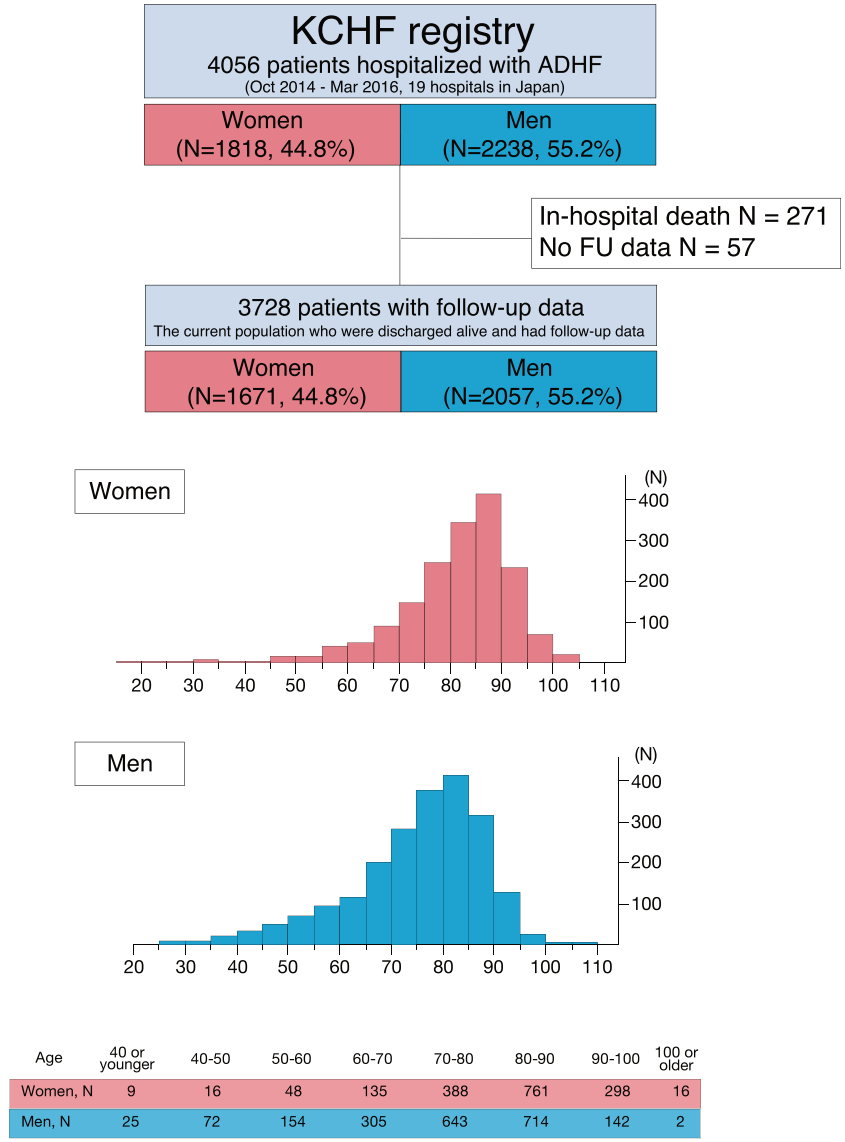
Patient characteristics

Among 4056 patients enrolled in the KCHF registry, 271 patients died during the index hospitalization [women: 123 patients (6.8%) and men: 148 patients (6.6%)]. Among 3785 patients who were alive at discharge, 57 were excluded because of missing follow-up data after discharge. Finally, 3728 patients (women: 1671 patients and men: 2057 patients) were included in the present analysis comparing the baseline characteristics and clinical outcomes between men and women (*Figure 1*). Women were significantly older than men (83 [76–88] years vs. 77 [68–84] years, $P < 0.0001$). Atrial fibrillation and dementia were more frequently observed in women than in men. The prevalence of hypertension and dyslipidemia was not significantly different between the sexes. However, diabetes, CKD, chronic obstructive pulmonary disease, and prior heart disease were more frequently observed in men than in women. Regarding the underlying heart disease, hypertensive and valvular heart diseases were more frequently observed in women than in men, whereas ischaemic aetiology with elevated troponin values (Supporting Information, *Table S1*) was more frequently observed in men than in women. During the hospitalization, men more frequently required NPPV and intubation than women. Men also required inotropes and intra-aortic balloon pump more frequently than women. ICD and CRT device implantations were more frequently observed in men. Preserved LVEF was significantly frequently observed in women than in men. As for the social background, 35% of men were living with their spouses, while the proportion of women who were living with their spouses was only 16%; furthermore, there were more women than men who were living alone, in institutions for aged people, or in hospitals. Furthermore, women more frequently used wheelchair or were bedridden than men (*Table 1* and Supporting Information, *Table S1*).

One-year outcome: women vs. men

The 1-year follow-up rate was 98.5%. The cumulative incidence of the primary outcome measure (composite of

Figure 1 Study flowchart. ADHF = acute decompensated heart failure, KCHF = Kyoto Congestive Heart Failure.



Age	40 or younger	40-50	50-60	60-70	70-80	80-90	90-100	100 or older
Women, N	9	16	48	135	388	761	298	16
Men, N	25	72	154	305	643	714	142	2

all-cause death or hospitalization for HF) was not significantly different between women and men (33.6% vs. 34.3%, log-rank P = 0.71) (*Figure 2A* and *Table 2*). After adjusting confounders, the risk for the primary outcome measure was significantly lower in women than in men (*Table 2*). The cumulative incidence of secondary outcome measures was also not significantly different between the sexes (all-cause death: 16.3% vs. 17.9%, log-rank P = 0.26, cardiac death: 10.6% vs. 10.6%, log-rank P = 0.98, and HF hospitalization: 24.3% vs. 23.9%, log-rank P = 0.82) (*Figure 2DB2*). However, after adjusting confounders, the risks for all-cause death and cardiac death were significantly lower in women than in men (adjusted hazard ratio: 0.84, 95% confidence interval: 0.74–0.96, P = 0.01), while the risk for HF hospitalization was neutral between women and men (*Table 2*).

Subgroup analysis

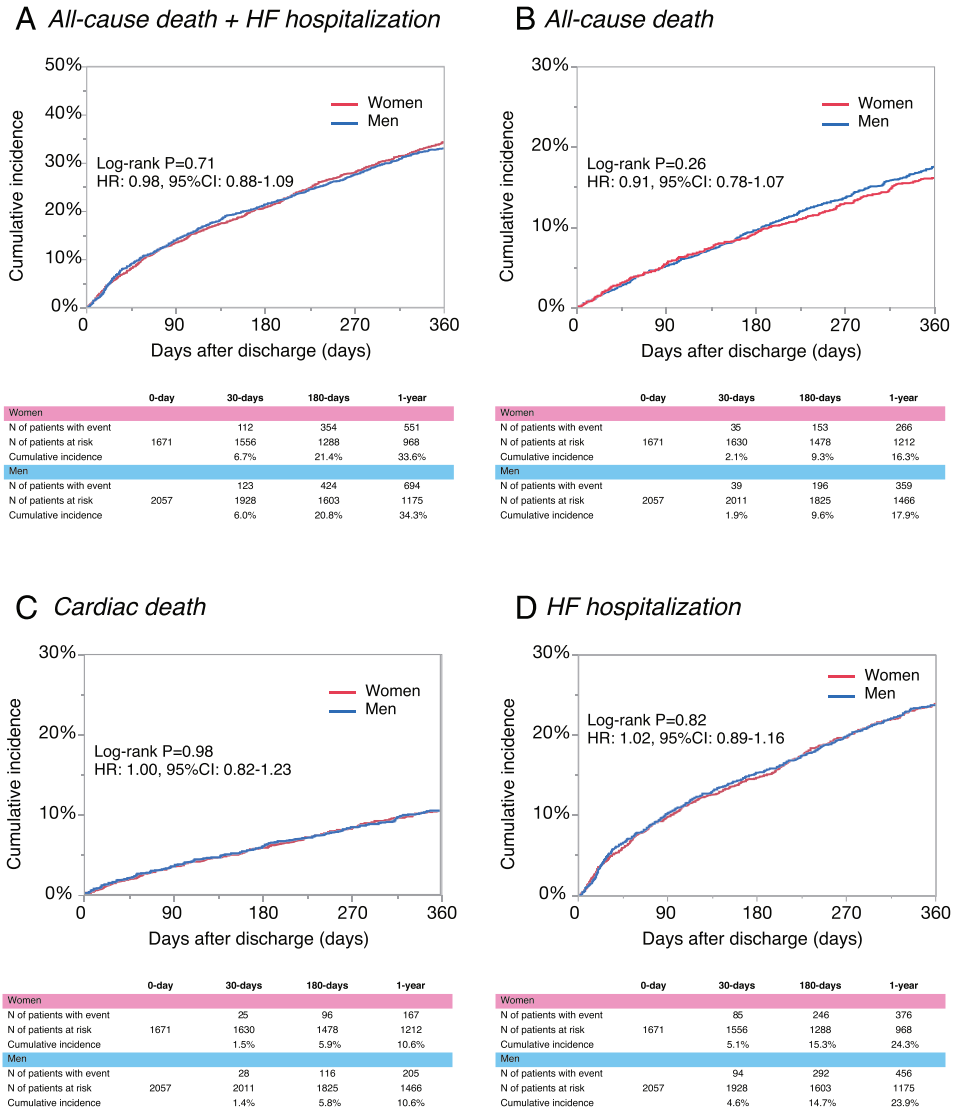
In the subgroup analysis, no interactions were observed between the subgrouping factors and the risk of women relative to men on the primary outcome measure (*Figure* 3).

Discussion

The main findings of this study were as follows: (i) Women with HF were older and more often presented with preserved EF with a non-ischaemic aetiology compared with men. (ii) Atrial fibrillation and dementia were more frequently observed in women than in men. (iii) More women were

DOI: 10.1002/ehf2.12815

Figure 2 Kaplan–Meier curves for (A) the primary endpoint (a composite of all-cause death or heart failure hospitalization), (B) all-cause death, (C) cardiac death, and (D) HF hospitalization. HR = hazard ratio, CI = confidence interval, HF = heart failure.



	0-day	30-days	180-days	1-year
Women				
N of patients with event		112	354	551
N of patients at risk	1671	1556	1288	968
Cumulative incidence		6.7%	21.4%	33.6%
Men				
N of patients with event		123	424	694
N of patients at risk	2057	1928	1603	1175
Cumulative incidence		6.0%	20.8%	34.3%

	0-day	30-days	180-days	1-year
Women				
N of patients with event		35	153	266
N of patients at risk	1671	1630	1478	1212
Cumulative incidence		2.1%	9.3%	16.3%
Men				
N of patients with event		39	196	359
N of patients at risk	2057	2011	1825	1466
Cumulative incidence		1.9%	9.6%	17.9%

	0-day	30-days	180-days	1-year
Women				
N of patients with event		25	96	167
N of patients at risk	1671	1630	1478	1212
Cumulative incidence		1.5%	5.9%	10.6%
Men				
N of patients with event		28	116	205
N of patients at risk	2057	2011	1825	1466
Cumulative incidence		1.4%	5.8%	10.6%

	0-day	30-days	180-days	1-year
Women				
N of patients with event		85	246	376
N of patients at risk	1671	1556	1288	968
Cumulative incidence		5.1%	15.3%	24.3%
Men				
N of patients with event		94	292	456
N of patients at risk	2057	1928	1603	1175
Cumulative incidence		4.6%	14.7%	23.9%

living alone than men, and activities of daily living were more impaired in women. (iv) Although the crude incidence of in-hospital mortality and primary outcome measure (composite of all-cause death and hospitalization for HF) was not significantly different between the sexes, the lower risk of women relative to men for the primary outcome measure, all-cause death, and cardiac death was significant after adjusting for confounders.

Sex differences in patient characteristics at hospital presentation

Consistent with previous reports, women were significantly older than men in the present study. This finding reflects the rapidly ageing society in Japan; in fact, the mean age of women in this study reached 83 years, which is significantly older than that in other studies conducted outside Japan. In addition, the present study revealed significant differences in the social background between women and men. Ambulatory patients were less often observed in women than in men. These situations may not be limited to patients with HF. Thus, women are, theoretically, more likely to be isolated in society than men. Women living with their spouses only were significantly less than men, indicating that women with HF were likely to live with their family members or in institutions for the aged after their partner died. A previous study has reported living alone as a risk factor for the development of disability after adjustment for health and other covariates, especially in women.[19] Therefore, the management of

Table 2 Clinical outcomes (1 year)

Outcome	Women			Men						
	N of patients with event/*N* of patients	Cumulative 1-year incidence		*N* of patients with event/*N* of patients	Cumulative 1-year incidence	Unadjusted			Adjusted	
						HR	95%CI	*P* value	HR	95%CI	*P* value
Primary endpoint A composite of all-cause death or HF hospitalization	551/1671	33.6%		694/2057	34.3%	0.98	0.98–1.09	0.71	0.84	0.74–0.96	0.01
Secondary endpoint											
All-cause death	266/1671	16.3%		359/2057	17.9%	0.91	0.78–1.07	0.26	0.63	0.52–0.76	<0.0001
Cardiac death	167/1671	10.6%		205/2057	10.6%	1.00	0.82–1.23	0.98	0.70	0.55–0.89	0.004
HF hospitalization	376/1671	24.3%		456/2057	23.9%	1.02	0.89–1.16	0.82	0.97	0.83–1.14	0.76

HR, hazard ratio; CI, confidence interval; HF, heart failure.

medication, awareness of the living status and support outside hospital, and physical activities of daily living are crucial factors for the management of patients with ADHF, especially for aged women.

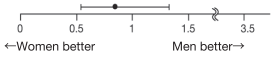
Sex differences in the 1-year outcome

The lower risk of women than men for all-cause death may be explained by the effect of oestrogen, which has an anti-atherosclerotic effect; therefore, the incidence of ischaemic heart diseases is significantly lower before menopause.[20] In a Japanese large cohort database, the age of onset of myocardial infarction is 8 years older in women than in men.[21] Therefore, the preserved EF and a non-ischaemic aetiology might have been related to a better outcome in women.[22,23] In contrast, some studies have demonstrated that the favourable effect of women is no longer valid if HF was caused by an ischaemic aetiology.[24] In the present study, the lower risk of women for 1-year outcomes remained significant even in patients with low LVEF, ischaemic aetiology, or >80 years of age. No interactions were observed between the subgroup factors and the risk of women relative to men for the primary outcome measures. These results suggest that inherent mechanisms that protect women from mortality work well in patients with ADHF as they work in the general population. Besides the oestrogen theory, the vascular response to salt intake and angiotensin II is different between women and men,[25] although the precise mechanisms of sex differences are still under investigation.

Notably, implantable device (ICD/cardiac resynchronization therapy defibrillator/cardiac resynchronization therapy pacemaker) were less common in this registry than European and American registries. First of all, ischaemic aetiology was less common in Japanese population than European and American population; therefore, implantation of defibrillator for secondary prevention of VT/Vf with CAD was fewer in Japan than other countries. In addition, the preserved EF was more frequently observed in this registry than other European and American registries, therefore implantation of CRT device should also be fewer in Japan then other registries (Supporting Information, *Table S2*). Although the proportion of these implantable devices was low, there is still significant difference in defibrillator use between genders, which is consistent with prior studies in Western countries.[26] The reasons for sex differences in ICD use remain largely unknown, but in the study enrolling 21 059 patients admitted with HF and an ejection fraction ≤ 35% without an ICD, women were counselled for ICD implantation less often than men.[27] Although there is a relevant difference to comparable European or American HF cohorts, the benefit of women compared with men remained significant after multivariable adjustment including age, comorbidities, and the use of implantable devices.

Figure 3 Subgroup analysis for the effect of sex difference on the primary endpoint. DM = diabetes mellitus, LVEF = left ventricular ejection fraction, HR = hazard ratio, CI = confidence interval.

	Women		Men					
	N of patients with event /N of patients at risk	Cumulative 1-year incidence	N of patients with event /N of patients at risk	Cumulative 1-year incidence	HR	95%CI	*P*	*P* for interaction
Acute coronary syndromes	18/72	25.8%	24/134	17.9%	1.45	0.60-3.52	0.41	0.42
Ischemic etiology (non acute)	132/334	40.1%	270/669	40.8%	0.91	0.71-1.14	0.41	
Non-ischemic etiology	401/1265	32.2%	400/1254	32.6%	0.80	0.68-0.94	0.006	
Valvular	160/449	36.5%	106/288	37.4%	0.88	0.66-1.17	0.37	0.82
Non-valvular	391/1222	32.5%	588/1769	33.9%	0.83	0.72-0.96	0.01	
Hypertensive	128/467	27.8%	154/462	34.2%	0.72	0.55-0.95	0.02	0.06
Non-hypertensive	423/1204	35.9%	540/1595	34.4%	0.90	0.78-1.05	0.18	
DM	197/544	36.9%	302/853	36.0%	0.93	0.76-1.14	0.48	0.25
Non-DM	354/1127	32.0%	392/1204	33.2%	0.79	0.67-0.94	0.008	
Age >= 80years	416/1075	39.6%	374/858	44.4%	0.93	0.79-1.10	0.410	0.13
Age < 80years	135/596	22.9%	320/1199	27.2%	0.71	0.56-0.88	0.00	
Living alone	110/379	29.6%	116/417	29.0%	0.84	0.62-1.15	0.28	0.85
Living with someone	441/1292	34.8%	578/1640	35.7%	0.85	0.73-0.98	0.02	
Ambulatory	342/1207	28.8%	518/1742	30.3%	0.84	0.72-0.98	0.03	0.80
Non-ambulatory	206/444	47.7%	167/297	57.5%	0.88	0.69-1.14	0.33	
LVEF >= 40%	388/1210	32.6%	361/1124	32.7%	0.84	0.71-0.99	0.03	0.94
LVEF < 40%	163/458	36.3%	330/925	36.3%	0.85	0.68-1.05	0.16	
Troponin high	95/249	38.7%	102/315	32.6%	1.06	0.78-1.46	0.70	0.24
Troponin low	47/209	22.8%	34/237	27.4%	0.85	0.54-1.33	0.47	



Interestingly, the risk of women relative to men for rehospitalization for HF was not significant after adjusting for confounders, which may be due to the following two reasons: (i) The triggers to the exacerbation of HF, such as anaemia, fever, and infection, were unavoidable in the aged patients; thus, the risk of rehospitalization for HF was comparable between the sexes. (ii) Social background and cognitive dysfunction observed in the aged women might be related to their lower threshold for hospitalization. This may be counterbalanced by the biological benefit of female gender to live longer. Therefore, support systems after discharge, including cooperation of family members and health care providers at hospital and caregiving sites, would become increasingly important for the management of patients with HF and for reduction of rehospitalizations for HF in the super-ageing society.

Limitations

There were several limitations in the present study. First, this was an observation study; therefore, unmeasured confounders that affect mortality might be present. Second, responses to the medication or treatment might be different between men and women; however, we did not directly compare these responses between the sexes.

Conclusions

Women with HF were older and more often presented with preserved EF with a non-ischaemic aetiology and were associated with a reduced adjusted risk of 1-year mortality compared with men in the Japanese population.

Conflict of interest

None declared.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. Troponin T and I values.
Table S2. Previous representative ADHF registries and KCHF registry.

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