Association of Previous Hospitalization for Heart Failure With Increased Mortality in Patients Hospitalized for Acute Decompensated Heart Failure

Kanae Su, MD; Takao Kato, MD; Mamoru Toyofuku, MD; Takeshi Morimoto, MD;
Hidenori Yaku, MD; Yasutaka Inuzuka, MD; Yodo Tamaki, MD; Neiko Ozasa, MD;
Erika Yamamoto, MD; Yusuke Yoshikawa, MD; Yasuyo Motohashi, MD;
Hiroki Watanabe, MD; Takeshi Kitai, MD; Ryoji Taniguchi, MD; Moritake Iguchi, MD;
Masashi Kato, MD; Kazuya Nagao, MD; Takafumi Kawai, MD; Akihiro Komasa, MD;
Ryusuke Nishikawa, MD; Yuichi Kawase, MD; Takashi Morinaga, MD; Toshikazu Jinnai, MD;
Mitsunori Kawato, MD; Yukihito Sato, MD; Koichiro Kuwahara, MD;
Takashi Tamura, MD; Takeshi Kimura, MD; KCHF Registry Investigators

Supplementary Table 1. Patient characteristics of the study population in the additional analysis

Variables	Previous hospitalization group (N=1321, 35.4%)	De novo hospitalization group (N=2407, 64.6%)	P value
Clinical characteristics			
Age, years	81 [73-86]	79 [71-86]	0.0006
Age >80 years*	740 (56.0)	1193 (50.0)	0.0002
Men*	718 (54.4)	1339 (55.6)	0.47
BMI$^{\parallel}$, kg/m^2	21.9 [19.7-25.0]	25.6 [20.1-22.6]	0.0015
BMI<22 kg/m^2*	646 (50.3)	993 (43.7)	0.0002
Etiology			<0.001
Cardiomyopathy	223 (16.99	334 (13.9)	
Dilated cardiomyopathy	155 (11.7)	246 (10.2)	
Valvular heart disease	279 (21.1)	458 (19.0)	
Hypertensive	269 (20.4)	660 (27.4)	
Ischemic	427 (32.3)	576 (23.9)	
Associated with ACS *	29 (2.2)	177 (7.4)	
Not associated with ACS	1292 (97.8)	2230 (92.7)	
Arrhythmia-related	40 (3.0)	139 (5.8)	
Others	43 (3.3)	56 (2.3)	
Medical history			
Atrial fibrillation or flutter*	694 (52.5)	862 (35.8)	<0.0001
Hypertension*	940 (71.2)	1759 (73.1)	0.22
Diabetes mellitus*	554 (41.9)	843 (35.0)	<0.0001
Dyslipidemia	587 (44.4)	868 (36.1)	<0.0001
Prior myocardial infarction*	411 (31.1)	427 (17.7)	<0.0001
Prior stroke*	225 (17.0)	368 (15.3)	0.17
Prior PCI or CABG	505 (38.2)	451 (18.7)	<0.0001
Current smoking*	123 (9.5)	330 (14.0)	<0.0001
Ventricular tachycardia/fibrillation	101 (7.7)	54 (2.2)	<0.0001
Chronic lung disease*	755 (75.2)	889 (36.9)	<0.0001

Liver cirrhosis	186 (14.1)	303 (12.6)	0.25
Malignancy	14 (1.1)	32 (1.3)	0.54
Dementia	202 (15.3)	335 (13.9)	0.26
Social backgrounds			
Poor medical adherence	251 (19.0)	378 (15.7)	0.0105
Living alone*	275 (20.8)	521 (21.7)	0.59
With occupation	119 (9.0)	375 (15.6)	<0.0001
Public financial assistance	94 (7.1)	124 (5.2)	0.016
Daily life activities			
Ambulatory*	1068 (74.9)	2081 (80.4)	<0.001
Use of wheelchair [outdoor only]	138 (9.7)	167 (6.5)	<0.001
Use of wheelchair [outdoor and indoor]	165 (11.6)	223 (8.6)	0.003
Bed-ridden	55 (3.9)	117 (4.5)	0.33
Vital signs at presentation			
Systolic blood pressure, mmHg	143 ± 34	151 ± 35	<0.0001
Systolic blood pressure <90 mmHg*	45 (3.4)	50 (2.1)	0.016
Heart rate, bpm	92 ±25	98 ± 29	<0.0001
Heart rate <60 bpm*	66 (5.0)	186 (7.8)	0.0016
NYHA Class III or IV	1150 (87.5)	2081 (86.8)	0.61
Tests at admission			
LVEF	45.3 ± 16.6	46.9 ± 15.9	0.0033
LVEF <40%*	531 (40.3)	852 (35.5)	0.0041
BNP, pg/mL	745 [437-1294]	685 [375-1242]	0.012
Serum creatinine, mg/dL	1.3 [0.96-1.90]	1.0 [0.78-1.42]	<0.0001
eGFR <30 mL/min/1.73m^2*	487 (36.9)	497 (20.7)	<0.0001
Blood urea nitrogen, mg/dL	28 [20-41]	22 [17-31]	<0.0001
Sodium <135 mEq/L*	167 (12.7)	267 (11.1)	0.17
Anemia*§	989 (74.9)	1473 (61.4)	<0.0001
Albumin <3.0 g/dL*	165 (12.9)	317 (13.5)	0.65
Medications at discharge			
ACE-I or ARB*	724 (54.8)	1418 (58.9)	0.017
Beta blocker*	896 (67.8)	1577 (65.5)	0.16
MRA*	1146 (86.8)	1877 (78.0)	<0.0001

Loop diuretics*	231 (17.5)	161 (6.7)	<0.0001
Tolvaptan*	724 (54.8)	1418 (58.9)	0.017
Length of hospital stay	16 [11-25]	16 [12-24]	0.34

*25 risk-adjusting variables selected for multivariable COX proportional hazard models.

‖Body mass index was calculated as weight in kilograms divided by height in meters squared.

§Anemia was defined by the World Health Organization criteria (hemoglobin <12.0 g/dL in women and <13.0 g/dL in men).

BMI=body mass index; ACS=acute coronary syndrome, PCI=percutaneous coronary intervention; CABG=coronary artery bypass graft; BP=blood pressure; bpm=beat per minute; NYHA=New York Heart Association, LVEF=left ventricular ejection fraction; BNP=brain-type natriuretic peptide; eGFR=estimated glomerular filtration rate, ACE-I=angiotensin converting enzyme inhibitor, ARB=angiotensin receptor blocker, MRA=mineralocorticoid receptor antagonist.

Supplementary Table 2. Patient Characteristics in the 5 Groups Based on the Number of Hospitalization

Variables	None (N=2614, 64.5%)	Once (N=767, 18.9%)	Twice (N=277, 6.8%)	Three times (N=150, 3.7%)	Four times or more (N=248, 6.1%)	P value	Cochran-Armitage trend test
Clinical characteristics							
Age >80 years*	1326 (50.7)	436 (56.8)	161 (58.1)	86 (57.3)	138 (55.7)	0.005	0.003
Men*	1451 (55.5)	422 (55.0)	154 (55.6)	78 (52.0)	133 (53.6)	0.91	0.43
BMI <22 kg/m^2*	1069 (43.9)	362 (49.3)	147 (54.9)	78 (53.1)	131 (53.7)	<0.001	<0.001
Etiology							
Dilated cardiomyopathy	6.48 (10.1)	92 (12.0)	25 (9.0)	23 (15.3)	31 (12.5)	0.11	
Aortic stenosis	197 (7.5)	54 (7.0)	21 (7.6)	11 (7.3)	14 (5.7)	0.86	
Hypertensive	17.2 (26.6)	168 (21.9)	55 (19.9)	27 (18.0)	39 (15.7)	<0.001	
Ischemic	835 (32.0)	252 (32.9)	91 (32.8)	56 (37.3)	93 (37.5)	<0.001	
Associated with ACS*	206 (7.9)	22 (2.9)	4 (1.4)	2 (1.3)	5 (2.0)	<0.001	
Not associated with ACS	629 (24.1)	230 (30.0)	87 (31.4)	54 (36.0)	88 (35.5)	<0.001	
Medical history							
Atrial fibrillation or flutter*	925 (35.4)	378 (49.3)	144 (52.0)	86 (57.3)	148 (59.7)	<0.001	<0.001
Hypertension*	1900 (72.7)	553 (72.1)	200 (72.2)	98 (65.3)	158 (63.7)	0.02	0.002
Diabetes mellitus*	911 (34.9)	295 (38.5)	121 (43.7)	55 (36.7)	128 (51.6)	<0.001	<0.001
Dyslipidemia	924 (35.4)	321 (41.9)	124 (44.8)	61 (40.7)	119 (48.0)	<0.001	<0.001

Prior myocardial infarction*	467 (17.9)	213 (27.8)	86 (31.1)	56 (37.3)	86 (34.7)	<0.001	<0.001
Prior stroke*	417 (16.0)	125 (16.3)	48 (17.3)	26 (17.3)	46 (18.6)	0.83	0.23
Prior PCI or CABG	485 (18.6)	252 (32.9)	105 (37.9)	63 (42.0)	115 (46.4)	<0.001	<0.001
Current smoking*	346 (13.5)	77 (10.2)	25 (9.3)	11 (7.5)	17 (7.0)	0.001	<0.001
Ventricular tachycardia/fibrillation	56 (2.1)	46 (6.0)	17 (6.1)	16 (10.7)	30 (12.1)	<0.001	<0.001
Chronic lung disease*	322 (12.3)	102 (13.3)	48 (17.3)	28 (18.7)	36 (14.5)	0.04	0.01
Liver cirrhosis	39 (1.5)	5 (0.7)	3 (1.1)	0 (0.0)	8 (3.2)	0.02	0.51
Malignancy	365 (14.0)	122 (15.9)	47 (17.0)	17 (11.3)	34 (13.7)	0.34	0.86
Dementia	476 (18.2)	152 (19.8)	60 (21.7)	38 (25.3)	44 (17.7)	0.14	0.19
Social backgrounds							
Poor medical adherence	401 (15.3)	136 (17.7)	60 (21.7)	29 (19.3)	48 (19.4)	0.03	0.005
Living alone*	571 (21.8)	155 (20.2)	60 (21.7)	27 (18.0)	53 (21.4)	0.74	0.46
With occupation	389 (14.9)	77 (10.0)	22 (7.9)	11 (7.3)	11 (4.4)	<0.001	<0.001
Public financial assistance	131 (5.0)	46 (6.0)	14 (5.1)	8 (5.3)	35 (14.1)	<0.001	<0.001
Daily life activities							
Ambulatory*	2081 (80.4)	589 (77.7)	207 (75.6)	106(70.7)	166 (68.0)	<0.001	<0.001
Use of wheelchair [outdoor only]	167 (6.5)	59 (7.8)	29 (10.6)	17 (11.3)	33 (13.5)	<0.001	<0.001
Use of wheelchair [outdoor and indoor]	223 (8.6)	77 (10.2)	29 (10.6)	23 (15.3)	36 (14.8)	0.002	<0.001
Bedridden	117 (4.5)	33 (4.4)	9 (3.3)	4 (2.7)	9 (3.7)	0.70	0.22
Vital signs at presentation							
Systolic blood pressure <90 mmHg*	71 (2.7)	21 (2.8)	12 (4.4)	10 (6.7)	12 (4.9)	0.02	0.003

Heart rate <60 bpm*	193 (7.4)	32 (4.2)	18 (6.5)	6 (4.1)	16 (6.5)	0.02	0.09
NYHA Class III or IV	2270 (87.3)	667 (87.5)	249 (90.2)	137 (91.3)	214 (86.6)	0.39	0.40
Tests at admission							
LVEF <40%*	954 (36.7)	296 (38.6)	117 (42.4)	72 (48.3)	112 (45.3)	0.002	0.001
eGFR <30 mL/min/1.73m^2*	570 (21.9)	248 (32.3)	108 (39.1)	69 (46.0)	123 (49.8)	<0.001	<0.001
Sodium <135 mEq/L*	321 (12.3)	100 (13.1)	29 (10.5)	31 (20.8)	38 (15.4)	0.02	0.04
Anemia*	1627 (62.4)	556 (72.5)	212 (76.5)	114 (76.0)	196 (79.4)	<0.001	<0.001
Albumin<3.0g/dL*	379 (14.9)	93 (12.5)	41 (15.4)	20 (13.8)	34 (14.3)	0.58	0.62
Medications at admission							
ACE-I or ARB*	1100 (42.1)	401 (52.3)	153 (55.2)	66 (44.0)	130 (52.4)	<0.001	<0.001
Beta blocker*	720 (27.5)	416 (54.2)	160 (57.8)	95 (63.3)	169 (68.2)	<0.001	<0.001
MRA*	299 (11.4)	216 (28.2)	84 (30.3)	49 (32.7)	85 (32.7)	<0.001	<0.001
Loop diuretics*	853 (32.6)	551 (71.8)	236 (85.2)	123 (82.0)	213 (85.9)	<0.001	<0.001
Tolvaptan*	31 (1.2)	41 (5.4)	21 (7.6)	23 (15.3)	54 (21.8)	<0.001	<0.001

*25 risk-adjusting variables selected for multivariable COX proportional hazard models.
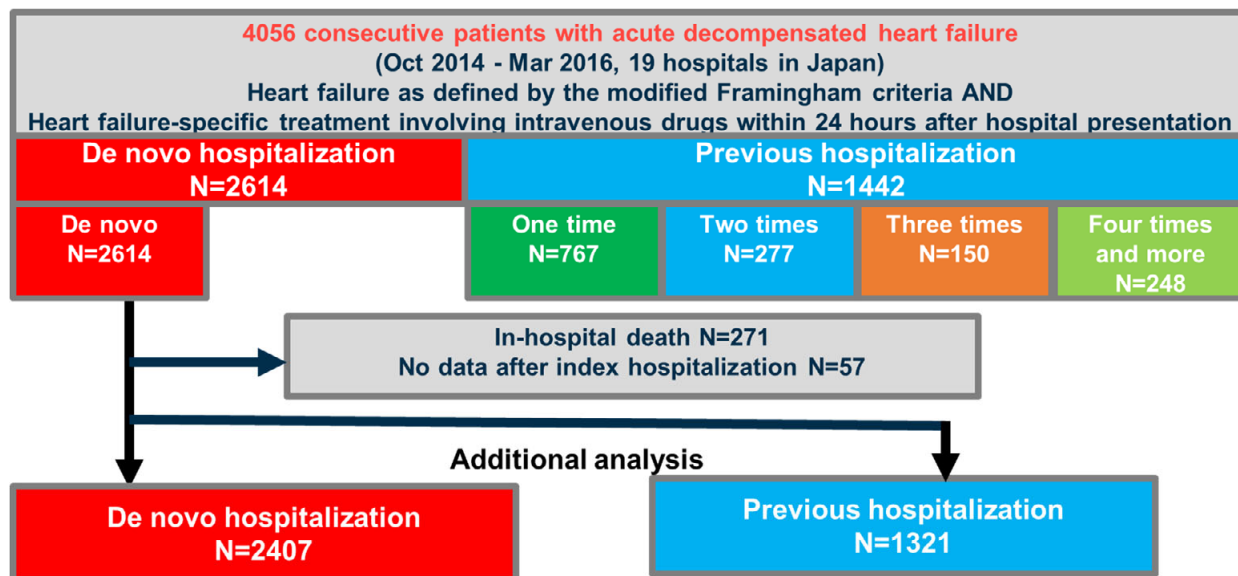
BMI=body mass index; ACS=acute coronary syndrome, PCI=percutaneous coronary intervention; CABG=coronary artery bypass graft; BP=blood pressure; bpm=beat per minute; NYHA=New York Heart Association, LVEF=left ventricular ejection fraction; BNP=brain-type natriuretic peptide; eGFR=estimated glomerular filtration rate, ACE-I=angiotensin converting enzyme inhibitor, ARB=angiotensin receptor blocker, MRA=mineralocorticoid receptor antagonist.

Supplementary Table 3. Clinical Outcomes of patients in the additional analysis

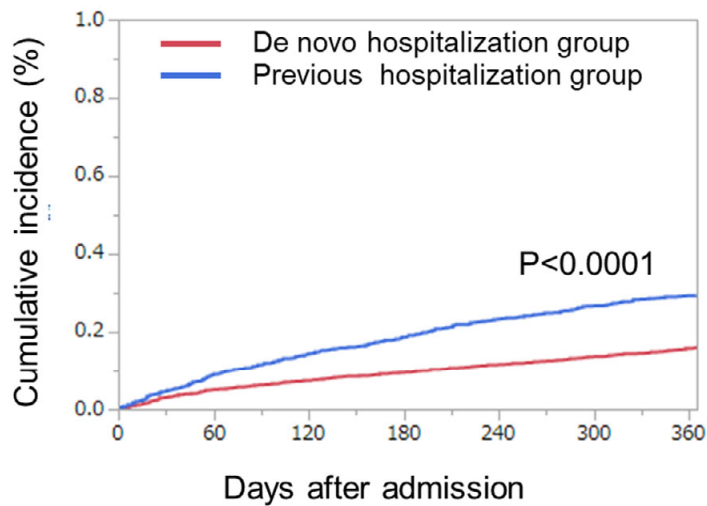|	Previous hospitalization	De novo	Unadjusted Hazard Ratio (95%CI)	P value	Adjusted Hazard Ratio (95%CI)	P value
	N of patients with event/N of patients at risk (Cumulative 1-year incidence [%])	N of patients with event/N of patients at risk (Cumulative 1-year incidence [%])				
All-cause death	387/1321 (29.3%)	465/2407 (15.9%)	1.86 (1.63-2.13)	<0.0001	1.27 (1.08-1.48)	0.0032

CI=confidence interval.

Supplementary Figure 1. Patient flowchart of the additional analysis.

Supplementary Figure 2. Cumulative incidences of all-cause death in the additional analysis (A) Previous hospitalization vs. de novo hospitalization. (B) Stratification by numbers of hospitalization.
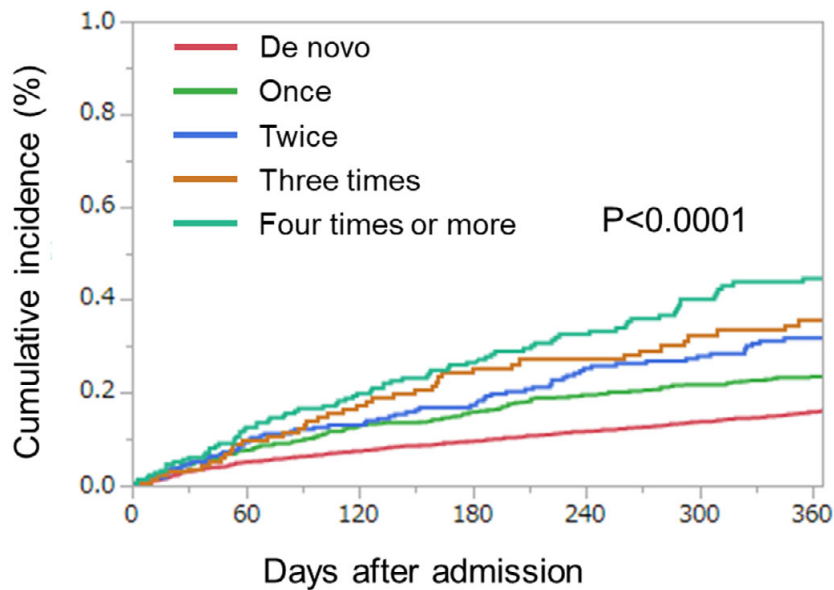
(A)

All-cause death

Interval	0 day	180 days	1 year
De novo hospitalization group			
N of patients with event		218	354
N of patients at risk	2407	1989	1575
Cumulative incidence (%)		9.5	15.9
Previous hospitalization group			
N of patients with event		227	337
N of patients at risk	1321	907	596
Cumulative incidence (%)		18.7	29.3

(B)

Interval	0 day	180 days	1 year
De novo hospitalization			
N of patients with event		218	354
N of patients at risk	2407	1989	1575
Cumulative incidence (%)		9.5	15.9
Once			
N of patients with event		106	150
N of patients at risk	713	528	371
Cumulative incidence (%)		15.8	23.4
Twice			
N of patients with event		39	67
N of patients at risk	248	170	108
Cumulative incidence (%)		17.2	31.6
Three times			
N of patients with event		30	41
N of patients at risk	137	83	52
Cumulative incidence (%)		24.3	35.7
Four times or more			
N of patients with at least 1 event		52	79
N of patients at risk	223	127	67
Cumulative incidence (%)		26.4	44.5