ESC HEART FAILURE
ESC Heart Failure 2021; **8**: 3002–3013
Published online 2 May 2021 in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/ehf2.13391

ORIGINAL RESEARCH ARTICLE

Early follow-up at outpatient care after discharge improves long-term heart failure readmission rate and prognosis

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Abstract

Aims It has been reported that congestive heart failure (CHF) readmission has not decreased in the last decade. It is also reported that CHF readmission is likely to occur shortly after discharge. We investigated whether an early follow-up at outpatient care within 2 weeks after discharge affects the long-term readmission rate and prognosis.

Methods and results We reviewed consecutive 1002 patients admitted to our hospital due to CHF. Two-hundred and fifty-nine patients who died in-hospital or were transferred to another hospital or readmitted within 2 weeks were excluded and 743 of discharged patients were analysed. We extracted contributing variables associated with heart failure (HF) readmission and the composite adverse outcome (all cause death or HF readmissions) by univariate and multivariate analysis. Multivariate analysis showed that the early follow-up was independently associated with freedom from HF readmission and the composite outcome. We divided these patients into two groups, with/without early follow-up and performed a propensity score-matching analysis (n = 259 each). HF readmission during 2 year follow-up was significantly less in the early follow-up group [P = 0.02, hazard ratio (HR) = 0.647, 95% confidence interval (CI) = 0.447–0.935] as well as the composite outcome was less in the early follow-up group (P = 0.01, HR = 0.643, 95% CI = 0.456–0.908). Medication adjustments were done in only 33.2% of the patients. Rates of HF readmissions were comparable regardless of whether or not medication adjustment was done at the early follow-up (P = 0.505, HR = 1.208, 95% CI = 0.692–2.106).

Conclusions The present study demonstrates that an early follow-up approach after discharge in CHF patients may improve the long-term prognosis. These results may not depend on medication adjustment but rather on modifying patient factors early after discharge.

Keywords Heart failure; Early follow-up; Heart failure readmissions

Received: 18 August 2020; Revised: 8 April 2021; Accepted: 13 April 2021
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Introduction

It is recognized that a heart failure (HF) pandemic is already in sight in Japan and worldwide. The majority of patients with HF are elderly with poor prognosis and requiring high economic burden.[1,2] The increasing of HF patients is a socio-economic problem and thus preventing HF readmission is an important medical and economic issue. Despite advances in treatment, the number of readmissions due to worsening HF has not decreased at all in the last decade.[3] Possible reasons for this result are patient factors such as insufficient salt restrictions, overwork, and poor compliance to the lifestyle guidance and medications.[4] It is reported that guideline-based medical therapy (GBMT) is not necessarily effective in elderly HF patients.[5] Thus, multidisciplinary interventions as well as GBMTs are important to reduce HF readmissions.[6–10] However, the clinical significance of multidisciplinary interventions to reduce HF readmission is still controversial.[11–13]

It is known that HF readmissions are likely to occur early after discharge, especially within a month.[14] It may be due

to changes in lifestyle, such as increasing salt intake and overwork early after hospital discharge. It is also reported that early follow-up at outpatient care 7 days after discharge reduce 30 days HF readmission.[15,16] Thus, early follow-up is thought to be effective in preventing HF readmissions; however, no reports have investigated its effect on the long-term outcomes. Thus, the aim of this study was to investigate the effects of early follow-up at outpatient care after initial hospital discharge on HF readmission and prognosis in a long-term.

Material and methods

Study design and patients

This is a single-centre, retrospective cohort study. Study design and number of patients are presented in *Figure 1*. We reviewed 1002 consecutive in-hospitalized patients due to decompensated HF from April 2015 to March 2019. Congestive HF was diagnosed on the basis of Framingham HF criteria.[17] After excluding the 196 patients transferred to another hospital, 39 patients died in-hospital and 24 patients readmitted within 2 weeks after discharge, and 743 patients were retrospectively investigated. The patients were followed up for 1 to 2 years after the initial hospital discharge. The median length of follow-up was 730 days (range, 16 to 730). The primary outcome was a readmission due to worsening HF. The secondary outcome was a composite of death from any cause or a HF readmission. Survival after discharge was confirmed from the follow-up records in our hospital or through direct telephone contact to each patient or their family members.

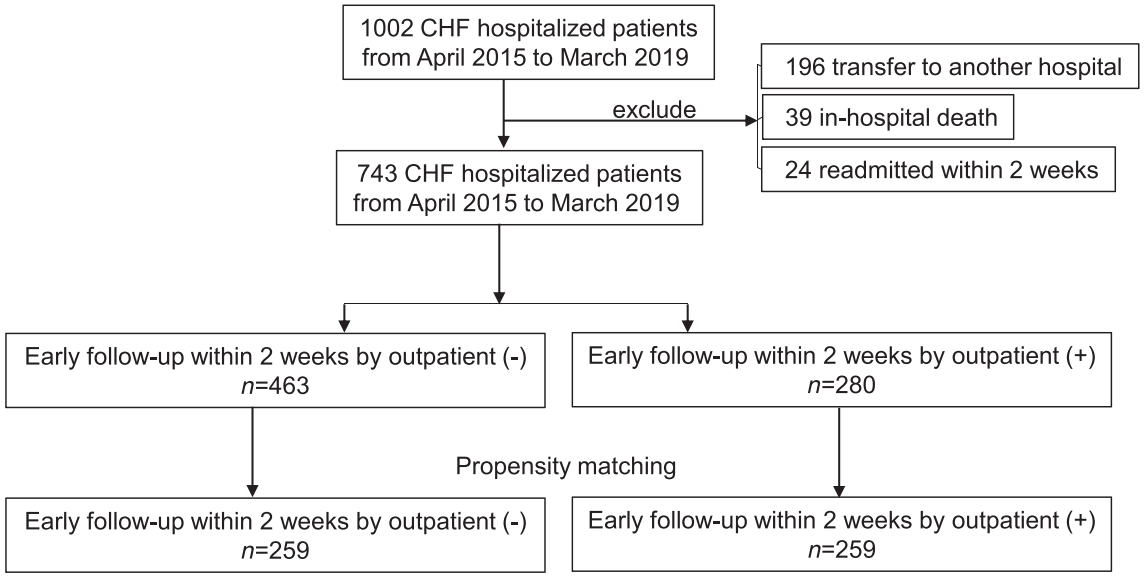
Extraction of factors associated with heart failure readmission and death

We investigated the factors associated with HF readmission and death by univariate and multivariate analyses. Patient backgrounds, comorbidities, laboratory data at admission (Labo data), treatment details during hospitalization (in hospital use), and prescription at discharge (use at discharge) were the analysed variables. Follow-up details after discharge were also analysed including early follow-up, number of visits to our outpatient department after first visit per year, continuation of outpatient rehabilitation, and follow-up by general practitioner (GP) (after discharge). Abbreviations are listed at the beginning of the text.

Association between early follow-up and long-term outcomes

We investigated the association between early follow-up and long-term clinical outcomes after propensity matching of patient characteristics. We defined early follow-up group as patients received a cardiologist and nurse-guided multidisciplinary follow-up at our outpatient department within 2 weeks after discharge. Non-early follow-up group was

Figure 1 Illustration of study design. CHF, congestive heart failure.



DOI: 10.1002/ehf2.13391

defined as patients other than the above mentioned. The early follow-up group includes patients who continue to be followed at our hospital with or without GP follow, and patients followed only by GPs after their first visit to our hospital. The non-early follow-up group includes patients followed in our hospital with or without GP follow and patients followed directly by GP after discharge. Whether to perform an early follow-up approach depended on the decision of each attending physician.

Contents of intervention at early follow-up at outpatient care

It was up to the attending physician to decide what to do in the early follow-up visit.

Regardless of whether it is an early follow-up visit or not, outpatient care at first visit to our hospital after discharge included medical examinations, lifestyle guidance and an adjustment of drugs as needed. A systematic lifestyle guidance such as salt reduction guidance, daily check of body weight, and avoidance of physical overload was performed by a cardiologist and/or a nurse. These were performed at our outpatient department, and we did not provide a telephone support by nurse. Contents of interventions were investigated in the 280 patients with early follow-up at outpatient care after discharge. Then, we investigated whether or not medication adjustments at early follow-up affected the outcomes.

Statistical analyses

All statistical analyses were performed with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). More precisely, it is a modified version of R commander designed to add statistical functions frequently used in biostatistics.[18]

Continuous variables in the early follow-up group/non-early follow-up group were compared using the unpaired *t*-test or Mann–Whitney test, as appropriate. Categorical variables among early follow-up group/non-early follow-up group were compared using the χ^2 test or Fisher's exact test, as appropriate. A univariate analysis about the factors associated with HF readmissions as well as the composite adverse outcome was performed using cox proportional hazards model. Then, a multivariate analysis using the cox proportional hazards model was performed. Independent variables used for multivariate analysis were selected with a P value < 0.05, and clinical variables likely to affect the outcomes were included. Then, we divided the patients into two groups: patients without early follow-up (n = 463) and patients with early follow-up (n = 280). There were many differences in the backgrounds between two groups. Thus, we performed a propensity score matching analysis. A propensity score indicating the predicted probability of early follow-up that was conditional on the observed covariates was calculated from the logistic equation for each patient. The following variables were included in the logistic regression model to calculate the propensity score: age, male, ejection fraction (EF), ischemic heart disease (IHD), frequent flyer (patients hospitalized for congestive HF at least twice in the past year), hospital stay, body mass index (BMI), pneumonia, blood urea nitrogen, estimated glomerular filtration rate (eGFR), uric acid, haemoglobin (Hb), albumin (Alb), catecholamine use, cardiac resynchronization therapy/implantable cardioverter defibrillator, angiotensin-converting enzyme inhibitor (ACE)/angiotensin receptor blocker, beta-blocker, mineralocorticoid receptor agonist (MRA), phosphodiesterase III inhibitor, sodium glucose co-transporter2 inhibitor, no. visits per year, outpatient rehabilitation, and follow-up by GP. We performed rigorous adjustment for significant differences in the baseline characteristics of patients matched by propensity score (n = 259 each). Clinical outcomes in the matched population were analysed by Kaplan–Meier curve with the log-rank test. Because some variables associated with HF readmission and the composite outcome remained with a difference, multivariate analysis using cox proportional hazards regression was added. Independent variables used for this multivariate analysis were as follows: catecholamine use, hospital stay, follow-up by GP, and early follow-up. Then, we investigated the contents of early outpatient care. Freedom from HF readmissions between the patients with or without medication adjustment in the early follow-up group were analysed by Kaplan–Meier curve with the log-rank test. Subgroup analysis was performed using a cox proportional hazard model. Unless otherwise specified, all data are expressed as the mean ± standard deviation or median [95% confidence interval (CI)]. The probability was two-tailed, with P values of <0.05 being regarded as statistically significant.

Ethical standards

All human and animal studies were approved by the appropriate ethics committee and were therefore performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. This study was approved by the ethics committee of Fukuoka Red Cross Hospital and got informed consent by an opt-out method.

Results

Studied patients

All patients backgrounds, comorbidities, laboratory data at admission (Labo data); treatment details during

hospitalization (in hospital use); prescription at discharge (use at discharge); and follow-up details after discharge (after discharge) are shown in *Table 1*.

Factors associated with heart failure readmissions and death

Results of the univariate and multivariate cox proportional hazard analyses to identify the clinical factors associated with HF readmissions and the composite outcome of HF re-admission or all-cause death are shown in *Table 2*. In the multivariate analysis, IHD and frequent flyer are independent positive predictive factors, whereas early follow-up was a negative independent predictive factor associated with HF readmissions. In terms of the composite outcome, IHD, frequent flyer, and chronic obstructive pulmonary disease were independent positive predictive factors, whereas early follow-up, higher Hb levels (>10.7 g/dL), and ACE inhibitor/angiotensin receptor blocker use were independent negative predictive factors. Early follow-up was a negative predictor for both HF readmission [P = 0.015, hazard ratio (HR) = 0.637, 95% CI = 0.443–0.916] and the composite outcome (P = 0.004, HR = 0.607, 95% CI = 0.431–0.856).

Propensity matching

The effect of early follow-up on HF readmissions and the composite outcome was further investigated. We divided 743 patients into two groups: early follow-up group and non-early follow-up group. The baseline characteristics of the two groups are presented in *Table 3* (left panel). In clinical characteristics, age is younger, more male patients are included, EF is lower, more IHD patients are included, longer hospital stay, less followed by GP, and BMI is higher in the early follow-up group. In laboratory data, eGFR, uric acid levels, Hb levels, and Alb levels is higher in the early follow-up group. In hospital use, catecholamine use was more prevalent in the early follow-up group. In use at discharge, beta-blocker use, MRA use and sodium glucose cotransporter2 inhibitor use are more in the early follow-up group. Because there were significant differences in characteristics between the two groups, a propensity score matching analysis was performed to eliminate the effects of related clinical factors (n = 259 each, *Table 3*, right panel).

The effect of early follow-up

The log-lank test demonstrated that HF readmission during 2 year follow-up was significantly less in the early follow-up group (P = 0.02, HR = 0.647, 95% CI = 0.447–0.935, *Figure 2A*) as well as the composite outcome was (P = 0.01, HR = 0.643, 95% CI = 0.456–0.908, *Figure 2B*). Readmission rate and readmission or death rate at 2 years follow-up were also lower in the early follow-up group compared with the non-early follow-up group (18.5 vs. 26.6%, 21.2 vs. 30.5%, P = 0.03). The total number of HF readmissions during the follow-up period were 1.44 ± 0.82 in the early follow-up group, and 1.22 ± 0.58 in the non-early follow-up group (P = 0.086) among patients who were readmitted at least once.

After matching, there were still some differences remained in the backgrounds. To reinforce the study results, we again performed multivariate cox proportional hazard analyses using the remained factors (catecholamine use, period of hospital stay, followed by GP, and early follow-up) in the matched groups. Longer hospital stay was an independent positive predictive factor, and early follow-up was an independent negative predictive factor associated with HF readmissions, showing the strongest significance and an HR of 0.586 for early follow-up. Catecholamine use and longer hospital stay were independent positive predictive factors, and early follow-up was an independent negative predictive factor associated with the composite outcome, showing the strongest significance and an HR of 0.577 for early follow-up. (Supporting Information, *Table S1*).

Subgroup analysis

We further performed subgroup analyses from the entire cohort to find out in which group of patient early follow-up approach is particularly effective. Early follow-up approach was more effective in younger than 75 years old, female, IHD, heart failure with reduced EF (HFrEF), non-invasive positive pressure ventilation use, shorter hospital stay (<19 days), de novo decompensated HF and followed by our own facility (*Figure 3*).

Intervention at early follow-up care

The first visit was at 8.9 ± 4.0 days after discharge in the early follow-up group and 56.2 ± 68.1 days in the non-early follow-up group. Contents of medication adjustment at early follow-up care are presented in *Table S2*. Lifestyle guidance was done in all patients. Medication adjustments were done in only 33.2% of the patients at the early follow-up visits. In the early follow group, HF readmissions were comparable between those with or without medication adjustments at the early follow-up visit (P = 0.505, HR = 1.208, 95% CI = 0.692–2.106, *Figure 4*).

Table 1 Characteristics of studied patients

Backgrounds	
Age	75.29 ± 13.76
Male (%)	468 (63.0)
BNP	916.6 ± 896.8
NYHA3,4 (%)	567 (76.3)
EF	40.9 ± 17.2
HFrEF (%)	369 (49.7)
HFmrEF (%)	117 (15.7)
HFpEF (%)	257 (34.6)
IHD (%)	262 (35.3)
Frequent flyer (%)	126 (17.0)
Hospital stay	19.9 ± 15.6
sBP	142.0 ± 35.5
dBP	82.0 ± 23.6
HR	90.3 ± 27.1
BMI	23.1 ± 4.9
Comorbidity	
AF (%)	326 (43.9)
DM (%)	285 (38.4)
COPD (%)	58 (7.8)
Dialysis (%)	55 (7.4)
Pneumonia (%)	85 (11.4)
Labo data	
BUN	29.9 ± 16.8
Cr	1.91 ± 2.00
eGFR	43.2 ± 23.5
UA	6.69 ± 2.08
Na	139.6 ± 4.0
K	4.40 ± 0.66
Hb	11.9 ± 2.48
Alb	3.64 ± 0.51
In hospital use	
Loop (%)	507 (68.3)
TLV (%)	219 (29.5)
Carperitide (%)	123 (16.6)
Catecholamine (%)	112 (15.1)
Vasodilator (%)	130 (17.5)
NPPV (%)	95 (12.8)
CRT/ICD (%)	27 (3.6)
Use at discharge	
ACEI/ARB (%)	605 (81.6)
BB (%)	567 (76.4)
MRA (%)	335 (44.1)
Anticoagulant (%)	322 (43.4)
Loop at discharge (%)	416 (56.0)
Loop dose (mg)	13.8 ± 16.6
TLV continue (%)	219 (29.5)
TLV dose (mg)	6.52 ± 3.38
PDE III i (%)	30 (4.0)
SGLT2i (%)	27 (3.6)
After discharge	
Early follow (%)	280 (37.7)
No. visits per year	4.02 ± 4.12
Outpatient rehabili (%)	66 (8.9)
Followed by GP (%)	457 (61.5)

Data are given as *n* (%) or the mean ± SD.

ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; AF, atrial fibrillation; Alb, albumin; BB, beta-blocker; BMI, body mass index; BNP, brain natriuretic peptide; BUN, blood urea nitrogen; COPD, chronic obstructive pulmonary disease; Cr, creatinine; CRT/ICD, cardiac resynchronization therapy/implantable cardioverter defibrillator; dBP, diastolic blood pressure; DM, diabetes mellitus; EF, ejection fraction; eGFR, estimated glomerular filtration rate; Followed by GP, patients followed by general practitioner after first visit; Frequent flyer, patients hospitalized for decompensated HF at least twice in the past year; Hb, haemoglobin; HF, heart failure; HFmrEF, HF with mid-range EF; HFpEF, HF with preserved EF; HFrEF, heart failure with reduced EF; HR, heart rate; IHD, ischemic heart disease; Loop, loop diuretics; MRA, mineralocorticoid receptor agonistNo. visits per year, Number of visits to our outpatient department after first visit per year; NPPV, non-invasive positive pressure ventilation; NYHA, New York Heart Association classification; Outpatient rehabili, patients performed outpatient rehabilitation; PDE III i, phosphodiesterase III inhibitor; sBP, systolic blood pressure; SGLT2i, sodium glucose cotransporter2 inhibitor; TLV, tolvaptan; UA, uric acid.

DOI: 10.1002/ehf2.13391

Table 2 Univariate and multivariate analyses associated with HF readmissions and with composite outcome

	Univariate analysis			Multivariate analysis		
	Hazard ratio	95% CI	*P* value	Hazard ratio	95% CI	*P* value
Analyses associated with HF readmissions						
Backgrounds						
Age	1.014	1.002–1.026	0.021	1.005	0.990–1.021	0.499
Male (%)	1.279	0.929–1.758	0.130	1.122	0.866–1.452	0.382
BNP	1.000	0.999–1.000	0.808	0.999	0.999–1.000	0.235
NYHA3,4 (%)	1.189	0.826–1.710	0.351	1.114	0.740–1.675	0.604
EF	0.997	0.989–1.006	0.585	0.995	0.982–1.008	0.478
HFrEF (%)	1.048	0.778–1.412	0.755			
HFmrEF (%)	1.080	0.720–1.619	0.707			
HFpEF (%)	0.912	0.665–1.251	0.570			
IHD (%)	1.902	1.412–2.564	<0.001	1.557	1.096–2.211	0.013
Frequent flyer (%)	2.368	1.700–3.300	<0.001	1.753	1.161–2.646	0.007
Hospital stay	1.010	1.003–1.018	0.005	1.008	0.997–1.018	0.123
sBP	0.996	0.991–1.000	0.081			
dBP	0.991	0.985–0.998	0.016	0.997	0.990–1.005	0.541
HR	0.997	0.991–1.003	0.283			
BMI	0.985	0.955–1.017	0.360			
Comorbidity						
AF (%)	1.188	0.881–1.601	0.257			
DM (%)	1.255	0.929–1.696	0.138	1.010	0.717–1.421	0.955
COPD (%)	1.543	0.958–2.485	0.074	1.390	0.816–2.367	0.224
Dialysis (%)	0.499	0.234–1.064	0.071	0.499	0.202–1.235	0.132
Pneumonia (%)	1.104	0.699–1.743	0.669			
Labo data						
BUN	1.009	1.001–1.017	0.027	0.998	0.984–1.007	0.791
Cr	0.979	0.906–1.058	0.599			
eGFR	0.992	0.985–0.998	0.018	0.995	0.984–1.007	0.436
UA	1.002	0.932–1.077	0.952			
Na	1.010	0.973–1.049	0.591			
K	0.902	0.713–1.141	0.389			
Hb	0.898	0.845–0.955	<0.001	0.921	0.847–1.002	0.056
Alb	0.765	0.577–1.014	0.06			
In hospital use						
Loop (%)	1.290	0.924–1.800	0.133			
TLV (%)	1.940	1.433–2.625	<0.001	1.237	0.789–1.936	0.353
Carperitide (%)	0.784	0.516–1.192	0.255			
Catecholamine (%)	1.615	1.119–2.331	0.010	1.167	0.712–1.912	0.539
Vasodilator (%)	0.867	0.578–1.300	0.49			
NPPV (%)	0.723	0.438–1.194	0.205			
CRT/ICD (%)	2.284	1.270–4.108	0.005	1.287	0.617–2.684	0.500
Use at discharge						
ACEI/ARB (%)	0.707	0.496–1.007	0.054	0.777	0.522–1.157	0.214
BB (%)	1.156	0.803–1.663	0.434	1.117	0.730–1.707	0.609
MRA (%)	1.022	0.758–1.379	0.884	1.120	0.795–1.575	0.516
Anticoagulant (%)	1.351	1.002–1.820	0.048	1.274	0.903–1.796	0.168
Loop at discharge (%)	1.221	0.900–1.655	0.199			
Loop dose (mg)	1.007	0.998–1.015	0.105	0.996	0.986–1.007	0.498
TLV continue (%)	2.190	1.558–3.078	<0.001	1.018	0.586–1.767	0.949
TLV dose (mg)	0.926	0.836–1.025	0.140			
PDE III i (%)	1.203	0.591–2.446	0.609			
SGLT2i (%)	0.782	0.321–1.904	0.588			
After discharge						
Early follow (%)	0.675	0.487–0.934	0.017	0.637	0.443–0.916	0.015
No. visits per year	1.009	0.972–1.047	0.628			
Outpatient rehabili (%)	1.208	0.732–1.994	0.459			
Followed by GP (%)	0.916	0.675–1.242	0.572			
Analyses associated with composite outcome						
Backgrounds						
Age	1.022	1.010–1.033	<0.001	1.014	0.999–1.030	0.062
Male (%)	1.060	0.860–1.306	0.582	1.113	0.893–1.387	0.340
BNP	1.000	0.999–1.000	0.734	0.999	0.999–1.000	0.412
NYHA3,4 (%)	1.415	0.998–2.006	0.051	1.279	0.864–1.891	0.218
EF	1.000	0.992–1.008	0.940	0.997	0.984–1.009	0.644
HFrEF (%)	0.996	0.757–1.3101	0.977			

(*Continues*)

Table 2 (continued)

	Univariate analysis			Multivariate analysis		
	Hazard ratio	95% CI	*P* value	Hazard ratio	95% CI	*P* value
HFmrEF (%)	1.084	0.746–1.573	0.672			
HFpEF (%)	0.989	0.742–1.318	0.939			
IHD (%)	1.911	1.453–2.514	<0.001	1.632	1.177–2.262	0.003
Frequent flyer (%)	2.365	1.740–3.213	<0.001	1.644	1.116–2.422	0.011
Hospital stay	1.011	1.005–1.018	<0.001	1.009	1.000–1.018	0.051
sBP	0.995	0.991–0.999	0.030	0.999	0.992–1.006	0.805
dBP	0.990	0.984–0.997	0.003	0.998	0.987–1.009	0.721
HR	0.996	0.991–1.001	0.153			
BMI	0.964	0.936–0.994	0.020	1.008	0.969–1.047	0.697
Comorbidity						
AF (%)	1.181	0.897–1.554	0.234			
DM (%)	1.345	1.021–1.772	0.035	1.126	0.822–1.543	0.458
COPD (%)	1.603	1.039–2.474	0.032	1.826	1.125–2.964	0.014
Dialysis (%)	0.670	0.365–1.231	0.197			
Pneumonia (%)	1.111	0.731–1.689	0.621			
Labo data						
BUN	1.008	1.001–1.016	0.027	0.991	0.978–1.004	0.180
Cr	0.986	0.920–1.057	0.696			
eGFR	0.991	0.985–0.997	0.003	0.996	0.986–1.006	0.468
UA	0.970	0.907–1.038	0.387			
Na	1.013	0.978–1.049	0.476			
K	0.908	0.731–1.129	0.387			
Hb (>10.7 g/dL)	0.870	0.822–0.920	<0.001	0.886	0.817–0.962	0.003
Alb	0.668	0.519–0.861	0.001	0.983	0.713–1.356	0.919
In hospital use						
Loop (%)	1.170	0.867–1.579	0.303			
TLV (%)	1.940	1.469–2.562	<0.001			
Carperitide (%)	0.900	0.623–1.303	0.579			
Catecholamine (%)	1.714	1.228–2.392	0.001	1.564	0.992–2.467	0.054
Vasodilator (%)	0.842	0.578–1.229	0.374			
NPPV (%)	0.631	0.389–1.024	0.062	0.626	0.372–1.054	0.077
CRT/ICD (%)	2.258	1.312–3.886	0.003	1.383	0.701–2.728	0.349
Use at discharge						
ACEI/ARB (%)	0.635	0.462–0.874	0.005	0.691	0.481–0.994	0.046
BB (%)	1.013	0.733–1.399	0.937	1.041	0.707–1.531	0.839
MRA (%)	1.001	0.760–1.317	0.995	1.126	0.818–1.551	0.465
Anticoagulant (%)	1.340	1.019–1.762	0.036	1.197	0.869–1.648	0.269
Loop at discharge (%)	1.230	0.930–1.627	0.145			
Loop dose (mg)	1.008	0.999–1.016	0.052	0.998	0.988–1.008	0.753
TLV continue (%)	2.363	1.733–3.222	<0.001	1.277	0.768–2.122	0.345
TLV dose (mg)	0.972	0.890–1.061	0.531			
PDE III i (%)	1.868	1.065–3.277	0.029	0.963	0.487–1.904	0.915
SGLT2i (%)	0.935	0.440–1.989	0.862			
After discharge						
Early follow (%)	0.620	0.458–0.838	0.001	0.607	0.431–0.856	0.004
No. of visits per year	0.986	0.953–1.021	0.447			
Outpatient rehabili (%)	1.125	0.701–1.804	0.626			
Followed by GP (%)	0.966	0.729–1.281	0.813			

Univariate and multivariate analyses using cox proportional hazard model was performed.
ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; AF, atrial fibrillation; Alb, albumin; BB, beta-blocker; BMI, body mass index; BNP, brain natriuretic peptide; BUN, blood urea nitrogen; COPD, chronic obstructive pulmonary disease; Cr, creatinine; CRT/ICD, cardiac resynchronization therapy/implantable cardioverter defibrillator; dBP, diastolic blood pressure; DM, diabetes mellitus; EF, ejection fraction; eGFR, estimated glomerular filtration rate; Followed by GP, patients followed by general practitioner after first visit; Frequent flyer, patients hospitalized for decompensated HF at least twice in the past year; Hb, haemoglobin; HF, heart failure; HFmrEF, HF with mid-range EF; HFpEF, HF with preserved EF; HFrEF, heart failure with reduced EF; HR, heart rate; IHD, ischemic heart disease; Loop, loop diuretics; MRA, mineralocorticoid receptor agonistNo. visits per year, Number of visits to our outpatient department after first visit per year; NPPV, non-invasive positive pressure ventilation; NYHA, New York Heart Association classification; Outpatient rehabili, patients performed outpatient rehabilitation; PDE III i, phosphodiesterase III inhibitor; sBP, systolic blood pressure; SGLT2i, sodium glucose cotransporter2 inhibitor; TLV, tolvaptan; UA, uric acid.

DOI: 10.1002/ehf2.13391

Table 3 Characteristics before and after propensity matching

	Before propensity matching			After propensity matching		
Characteristic *n*	Early follow (−) 463	Early follow (+) 280	*P* value	Early follow (−) 259	Early follow (+) 259	*P* value
Backgrounds						
Age	79.0 [29.0, 106.0]	76.0 [31.0, 100.0]	<0.001	74.6 ± 13.3	72.4 ± 14.8	0.069
Male (%)	269 (58.1)	199 (71.1)	<0.001	173 (66.8)	183 (70.7)	0.394
BNP	643.7 [23.3, 7712.9]	663.0 [5.8, 5320.9]	0.582	620.4 [23.3, 5121.0]	659.1 [5.8, 5320.9]	0.889
NYHA3,4 (%)	352 (76.0)	215 (76.8)	0.859	194 (74.9)	199 (76.8)	0.681
EF	42.9 ± 16.7	37.5 ± 17.4	<0.001	39.9 ± 16.7	37.5 ± 17.5	0.110
HFrEF (%)	209 (45.1)	160 (57.1)	0.002	139 (53.7)	149 (57.5)	0.426
HFmrEF (%)	75 (16.2)	42 (15.0)	0.679	37 (14.3)	37 (14.3)	1.000
HFpEF (%)	179 (38.7)	78 (27.9)	0.003	85 (32.8)	73 (28.2)	0.294
IHD (%)	181 (39.1)	81 (28.9)	0.006	91 (35.1)	73 (28.2)	0.108
Frequent flyer (%)	72 (15.6)	54 (19.3)	0.191	43 (16.6)	43 (16.6)	1.000
Hospital stay	16.0 [0.00, 120.0]	19.0 [2.0, 195.0]	<0.001	17.0 [1.0, 120.0]	19.0 [2.0, 195.0]	0.007
sBP	143.3 ± 36.1	139.9 ± 34.5	0.209	144.3 ± 39.3	141.3 ± 34.6	0.356
dBP	82.9 ± 36.6	82.9 ± 24.1	0.996	84.4 ± 25.0	83.6 ± 24.6	0.705
HR	89.5 ± 26.9	91.7 ± 27.4	0.298	93.7 ± 28.7	92.0 ± 28.0	0.513
BMI	22.2 [13.2, 48.0]	23.3 [10.0, 47.3]	0.001	23.0 [14.6, 48.0]	23.3 [10.0, 47.3]	0.304
Comorbidity						
AF (%)	205 (44.3)	121 (43.2)	0.819	112 (43.8)	111 (42.9)	1.000
DM (%)	182 (39.3)	103 (36.8)	0.534	98 (37.8)	97 (37.5)	1.000
COPD (%)	37 (8.0)	21 (7.5)	0.888	26 (10.0)	18 (6.9)	0.270
Dialysis (%)	39 (8.4)	16 (5.7)	0.195	17 (6.6)	14 (5.4)	0.712
Pneumonia (%)	64 (13.8)	21 (7.5)	0.009	27 (10.4)	20 (7.7)	0.359
Labo data						
BUN	30.4 ± 16.2	29.1 ± 17.7	0.294	29.0 ± 16.0	27.8 ± 16.4	0.409
Cr	1.20 [0.37, 14.05]	1.11 [0.45, 10.56]	0.136	1.85 ± 1.93	1.68 ± 1.73	0.293
eGFR	41.3 ± 23.6	46.3 ± 22.9	0.005	44.5 ± 24.1	47.3 ± 22.7	0.167
UA	6.5 ± 2.0	6.8 ± 2.1	0.04	6.66 ± 2.10	6.89 ± 2.12	0.23
Na	139.6 ± 4.0	139.5 ± 4.0	0.596	139.7 ± 4.3	139.6 ± 3.0	0.690
K	4.39 ± 0.66	4.43 ± 0.67	0.462	4.38 ± 0.68	4.39 ± 0.61	0.767
Hb	11.6 ± 2.3	12.4 ± 2.6	<0.001	12.2 ± 2.4	12.5 ± 2.64	0.209
Alb	3.58 ± 0.49	3.73 ± 0.52	<0.001	3.69 ± 0.47	3.73 ± 0.51	0.359
In hospital use						
Loop (%)	309 (66.7)	198 (71.0)	0.254	176 (63.8)	186 (71.8)	0.389
TLV (%)	134 (28.9)	85 (30.5)	0.678	83 (32.0)	77 (29.7)	0.635
Carperitide (%)	81 (17.5)	42 (15.1)	0.416	47 (18.1)	42 (16.2)	0.641
Catecholamine (%)	50 (10.8)	62 (22.2)	<0.001	35 (13.5)	53 (20.5)	0.046
Vasodilator (%)	82 (17.7)	48 (17.5)	0.921	50 (19.4)	44 (17.0)	0.496
NPPV (%)	57 (12.3)	38 (13.6)	0.650	37 (14.3)	32 (12.4)	0.605
CRT/ICD (%)	12 (2.6)	15 (5.4)	0.067	9 (3.5)	11 (4.2)	0.820
Use at discharge						
ACEI/ARB (%)	370 (79.9)	235 (84.2)	0.171	217 (83,8)	220 (84.9)	0.809
BB (%)	336 (72.6)	231 (82.8)	0.002	207 (79.9)	214 (82.6)	0.499
MRA (%)	194 (41.9)	141 (50.5)	0.023	117 (45.2)	134 (51.7)	0.159
Anticoagulant (%)	199 (43.0)	123 (44.1)	0.819	113 (43.6)	111 (42.9)	9.929
Loop at discharge (%)	260 (56.2)	156 (55.7)	0.939	145 (56.0)	143 (55.2)	0.930
Loop dose (mg)	13.6 ± 16.0	14.2 ± 17.5	0.659	10.0 [0.0, 80.0]	10.0 [0.0, 120.0]	0.956
TLV continue (%)	71 (15.3)	49 (17.5)	0.472	43 (16.6)	43 (16.6)	1.000
TLV dose (mg)	6.4 ± 3.3	6.6 ± 3.4	0.836	6.35 ± 3.24	6.22 ± 3.10	0.850
PDE III i (%)	14 (3.0)	16 (5.7)	0.083	11 (4.2)	11 (4.2)	1.000
SGLT2i (%)	10 (2.2)	17 (6.1)	0.008	7 (2.7)	16 (6.2)	0.086
After discharge						
No. visits per year	3.8 ± 4.3	4.3 ± 3.7	0.137	4.2 ± 4.3	4.5 ± 3.7	0.391
Outpatient rehabili (%)	36 (7.8)	30 (10.7)	0.185	19 (7.3)	27 (10.4)	0.280
Followed by GP (%)	322 (69.5)	135 (48.2)	<0.001	155 (59.8)	131 (50.6)	0.042

Data are given as *n* (%), the mean ± SD or the median plus confidence interval.
ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; AF, atrial fibrillation; Alb, albumin; BB, beta-blocker; BMI, body mass index; BNP, brain natriuretic peptide; BUN, blood urea nitrogen; COPD, chronic obstructive pulmonary disease; Cr, creatinine; CRT/ICD, cardiac resynchronization therapy/implantable cardioverter defibrillator; dBP, diastolic blood pressure; DM, diabetes mellitus; EF, ejection fraction; eGFR, estimated glomerular filtration rate; Followed by GP, patients followed by general practitioner after first visit; Frequent flyer, patients hospitalized for decompensated HF at least twice in the past year; Hb, haemoglobin; HF, heart failure; HFmrEF, HF with mid-range EF; HFpEF, HF with preserved EF; HFrEF, heart failure with reduced EF; HR, heart rate; IHD, ischemic heart disease; Loop, loop diuretics; MRA, mineralocorticoid receptor agonistNo. visits per year, Number of visits to our outpatient department after first visit per year; NPPV, non-invasive positive pressure ventilation; NYHA, New York Heart Association classification; Outpatient rehabili, patients performed outpatient rehabilitation; PDE III i, phosphodiesterase III inhibitor; sBP, systolic blood pressure; SGLT2i, sodium glucose cotransporter2 inhibitor; TLV, tolvaptan; UA, uric acid.

DOI: 10.1002/ehf2.13391

Figure 2 Survival curves of freedom from HF readmission (A) and HF readmissions and all-cause death (B) between the propensity matched patients with or without early follow-up after discharge by a Kaplan–Meier analysis. CI, confidence interval; HF, heart failure; HR, hazard ratio.

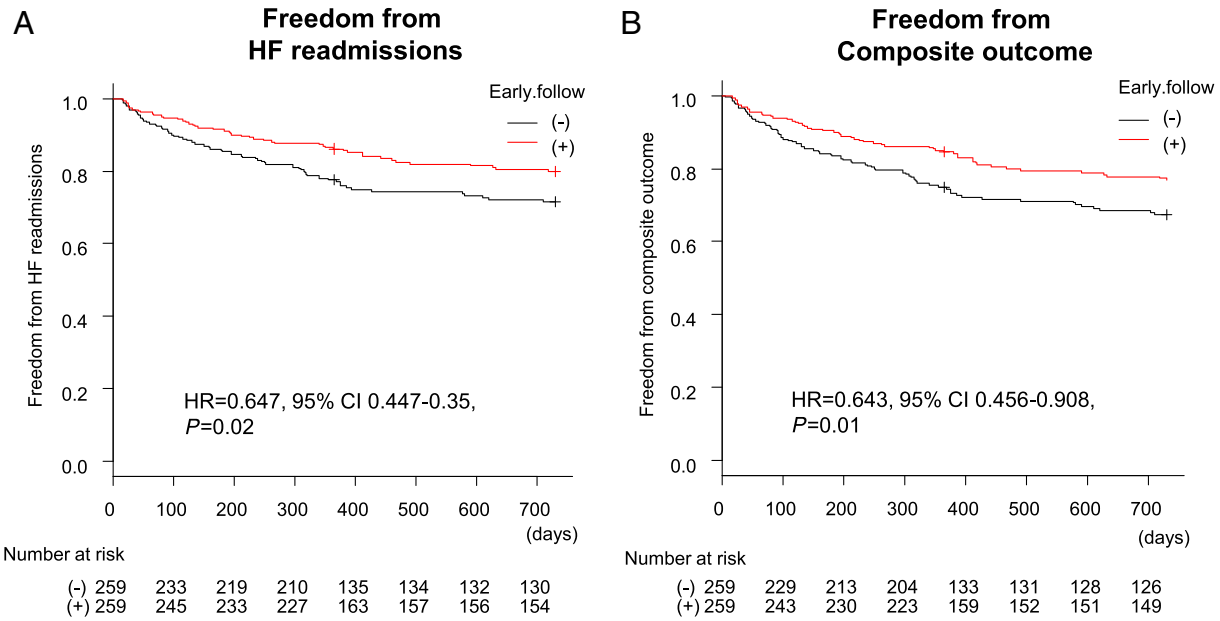


Figure 3 Subgroup analysis between patients with or without early follow-up after discharge by cox proportional hazard model presented by a forest plot. EF, ejection fraction; GP, general practitioner; HF, heart failure; HFmrEF, HF with mid-range EF; HFpEF, HF with preserved EF; HFrEF, heart failure with reduced EF; IHD, ischemic heart disease; NPPV, non-invasive positive pressure ventilation.

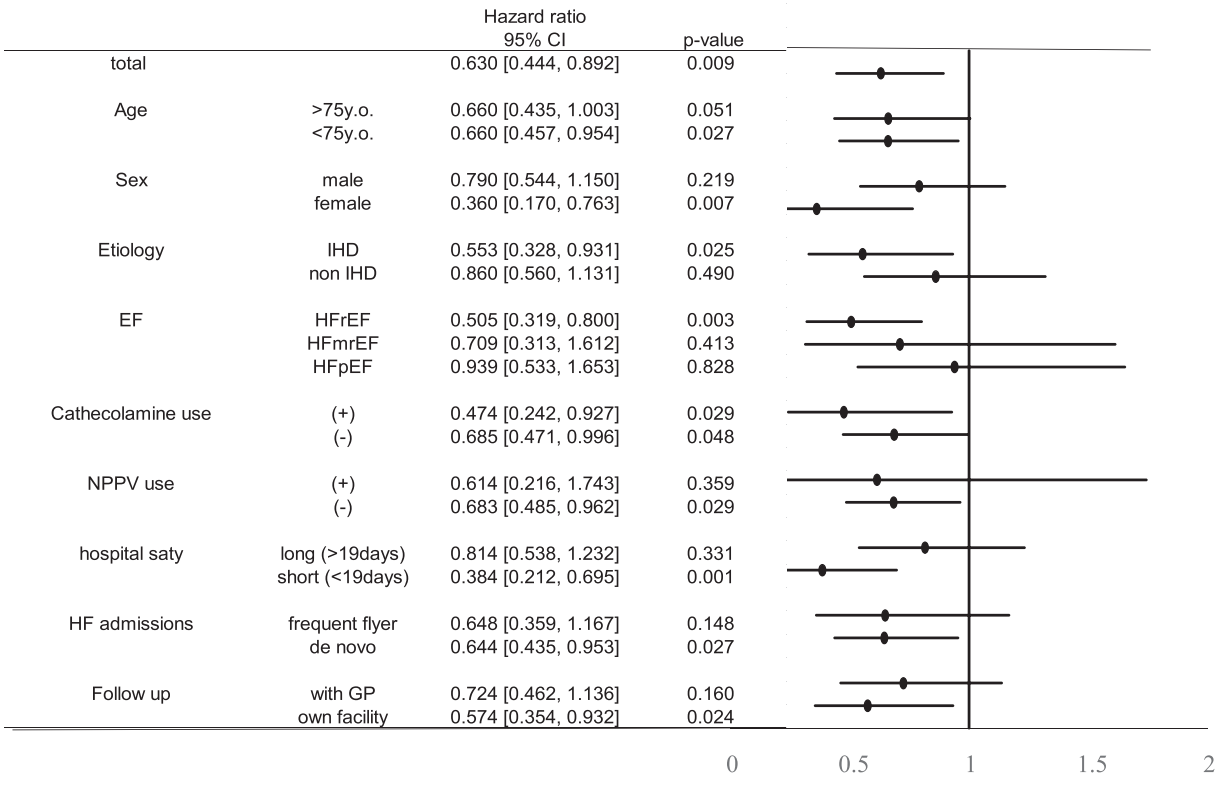
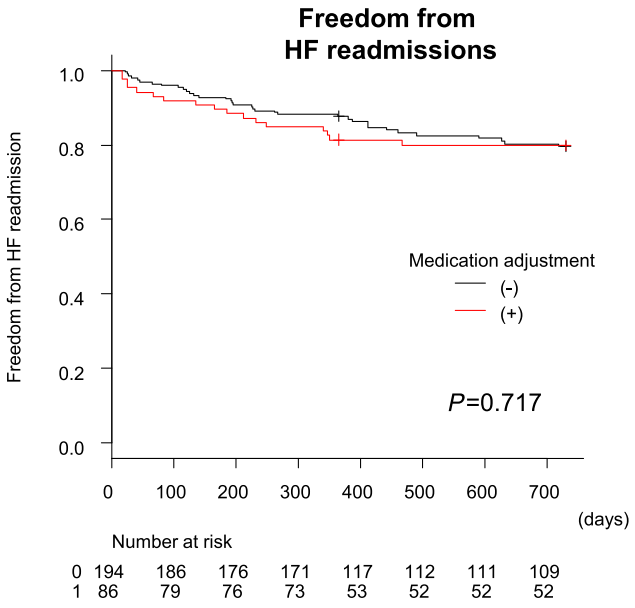


Figure 4 Survival curves of freedom from HF readmission between patients whether or not adjustment of medication was performed in early follow-up group by a Kaplan–Meier analysis. HF, heart failure.



Discussion

The present study demonstrated that early follow-up at outpatient care reduced HF readmissions and improved prognosis in CHF patients in a long-term. Although there have been reports of short-term efficacy of early follow-up approach for CHF patients,[14,15] this is the first report of long-term efficacy. At first, we showed that the early follow-up was an independent factor associated with a reduced long-term HF readmission rate and the composite adverse outcome. Then, we compared the patients groups with or without early follow-up regarding their prognosis. Comparing the backgrounds of the two groups, the early follow-up group included more patients of younger, male, higher BMI, low EF, IHD, pneumonia, longer hospital stay, less percentage followed by GP, higher eGFR, higher Hb, higher Alb, in-hospital catecholamine use, beta-blocker use at discharge, as well as MRA and SGLT2 inhibitor. The early follow-up group seemed to have a slightly higher proportion of severe illness but includes some factors that may be related to better prognosis such as more GBMT prescribed. Thus, we further performed a propensity score matching analysis to eliminate the effects of these confounding factors. After the propensity matching, the efficacy of early follow-up for long-term HF readmissions and prognosis robustly remained. These results demonstrate that early follow-up is associated with a reduction of HF readmissions and is improving the prognosis in CHF patients in a long-term.

We further investigated what kind of intervention was performed for patients in the early follow-up outpatient care and influenced the outcome. Regardless of whether it is an early follow-up visit or not, outpatient care at first visit to our hospital after discharge included medical examinations, lifestyle guidance, and an adjustment of drugs as needed. A systematic lifestyle guidance such as salt reduction guidance, daily check of body weight, and avoidance of physical overload was performed by a cardiologist and/or a nurse.

First, we considered that medication adjustments may have affected HF readmissions. Medication adjustments were done in only 33.2% of the patients in the early follow-up group. Further, whether or not medication adjustments were done at the early follow-up was not associated with the reduction in HF readmissions. These results suggest that adjustments of medications (i.e. titration of ACE inhibitor, beta-blocker, and MRA) or long-term follow-up by cardiologists may not be major causes of the favourable outcome in the early follow-up group. However, it was not possible to investigate changes in the medication during the subsequent follow-up period, which is a significant limitation of the present study.

Second, it may be possible that follow-up intensity and contents have influenced the outcome. A number of visits to our hospital and outpatient rehabilitation were not associated with HF readmission in the primary univariate analysis. Furthermore, there was no difference between the two groups with regards to the number of visits to our hospital and outpatient rehabilitation. Thus, it was probable that the effects of follow-up intensity and outpatient rehabilitation did not affect the results of the present study.

The mechanism by which an early follow-up approach was associated with the favourable outcomes remains to be clarified. Outpatient care at first visit to our hospital after discharge included medical examinations, systematic lifestyle guidance, and an adjustment of drugs as needed by a cardiologist and/or a nurse of a HF team. It has been reported that follow-up by cardiologists improved prognosis.[19,20] It is also known that HF readmissions are likely to occur early after discharge, especially within a month.[14] Previous reports demonstrated that early follow-up at outpatient care 7 days after discharge reduce 30 days HF readmission.[15,16] It is likely that an early follow-up approach provided as a HF team intervention during periods of high likelihood of re-exacerbation of HF resulted in favourable outcomes. However, this alone cannot explain the favourable long-term outcomes in the present study.

We considered the reason why an early follow-up approach brought the long-term effect. It was possible that continuous modifications of patient factors were brought by the early follow-up. By setting up an early follow-up outpatient care after discharge, patients may become aware of the fact that they will be immediately checked whether they are keeping with the instructed lifestyle guidance and drug adherence. As a result, patients themselves will be strongly aware of self-managements such as restriction of salt intake,

avoiding overwork, and daily-check of body weight after discharge. Another study has shown that self-management skills provided with educational methods do not persist without consistent follow-up and re-enforcement of education.[21] In the present study, patient education including lifestyle guidance had been started from the acute hospitalization period and was repeated in the follow-up visits. Contents at the first visit were not different between the early follow-up group and non-early follow-up group. It was probable that an early follow-up served as a key opportunity to immediately reconfirm the self-management learned during hospitalization, leading to a successful continuation of self-management. In other words, an early follow-up significantly influences patient factors in a long-term, and as a result, reduces HF readmissions and improves prognosis. HF readmissions have not decreased in the last decade partly because the patient factors that account for the majority of causes of HF readmissions are difficult to intervene. Our results indicated that an early follow-up after discharge may be one of a meaningful strategy to improve patient factors.

An early follow-up approach has been performed in only 37.6% of the patients in the present study. Although attending physicians feel its effectiveness, the reality is that they are not able to do it due to various reasons. Thus, we added subgroup analyses to find out in which patients we should recommend an early follow-up. The subgroup analyses showed that early follow-up approach seemed to be more effective in patients of: younger than 75 years, female, IHD, HFrEF, non-invasive positive pressure ventilation use, shorter hospital stay, de novo CHF, and follow-up by the own facility. It was possible that understanding and the effect of patient education in the early follow-up may be greater in younger and female patients. It was understandable that the educational effect of early follow-up would be high in those with shorter hospital stay and de novo CHF. Although the tendency of reduced risk with early follow-up was fairly preserved in a wide range of patient characteristics, mechanisms of greater reduction of HR observed in the subgroups of IHD and HFrEF remain to be further investigated. An early follow-up approach should be provided considering these patient backgrounds and situational factors.

Several limitations in the present study should be mentioned. First, this study is a single-centre retrospective cohort study. We therefore performed propensity score matching analysis in order to improve the statistical credibility. Second, whether or not early follow-up is performed depends on the judgement of the attending physician, so there is considerable selection bias in the present study. Third, changes in content of medication during the follow-up period may affect the results, but it is impossible to confirm them in the present study design. Further prospective study is needed.

In conclusion, the present study demonstrates that an early follow-up approach after discharge in congestive HF patients may improve the long-term prognosis. These results were not dependent on whether medication adjustment was performed. The early follow-up may be a leading strategy to improve patient factors that account for the HF worsening and readmissions.

Conflict of interest

There is no conflict of interest.

Funding

This research received no grant from any funding agency in the public, commercial, or not-for-profit sectors.

Supporting information

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

Table S1. Association with HF readmission and composite outcome after propensity matching.
Table S2. Medication adjustment at early follow-up care.

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