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ORIGINAL ARTICLE
Heart Failure

Clinical Impact and Associated Factors of Delayed Ambulation in Patients With Acute Heart Failure

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Background: In heart failure (HF) management, early ambulation is recommended to prevent physical deconditioning. The effects of delayed ambulation on later clinical outcomes and the factors linked to delayed ambulation in hospitalized HF patients, however, remain unestablished.

Methods and Results: We retrospectively investigated 101 patients (mean age, 66±17 years) who were hospitalized for acute decompensated HF. During the mean follow-up of 244±15 days after hospital discharge, 34 patients had cardiovascular events leading to death or unplanned readmission. Patients with cardiovascular events had longer median days to acquire ambulation than those without cardiovascular events (11 days, IQR, 8–20 days vs. 7 days, IQR, 5–15 days, P<0.001). The optimal cut-off period until initiation of ambulation to discriminate cardiovascular events was 8 days, indicating that longer days (≥8 days) to acquire ambulation was associated with higher rates of cardiovascular events, even after adjustment of multiple confounders. On multivariate analysis, age >65 years (odds ratio [OR], 2.49; 95% confidence interval [CI]: 1.04–6.09) and increase in blood urea nitrogen (BUN; OR, 1.04; 95% CI: 1.01–1.08) were independent predictors of delayed ambulation.

Conclusions: Delayed ambulation is associated with older age and increased BUN in patients with acute HF. Time to ambulation in the recovery phase of acute HF is important, and delayed ambulation may increase the rate of cardiovascular events after hospital discharge.

Key Words: Acute heart failure; Delayed ambulation; Older age; Physical deconditioning; Prognosis

The prevalence of heart failure (HF) has been increasing in elderly populations. Despite the development of medical and non-medical treatments for HF, many HF patients are repeatedly hospitalized for worsening HF and have poor prognosis.[1] Most patients are forced to bed rest in the acute phase of HF, but excess and long-term bed rest causes skeletal muscle atrophy due to physical deconditioning, and this leads to decrease in exercise capacity and in activities of daily living (ADL).[2,3] The early introduction of cardiac rehabilitation including exercise therapy can help HF patients achieve early ambulation from a state of bed rest. This may prevent decline in exercise capacity and improve quality of life, which is closely associated with an improvement in poor prognosis.[4] An objective index for achievement of early ambulation, however, has not been established, and a cardiac rehabilitation program for patients in the acute phase of HF has not been developed.

Many studies have clarified variables that can be used to predict mortality and cardiac events during hospitalization and after discharge in HF patients.[5–7] Low peak oxygen uptake, renal dysfunction, anemia, hyponatremia, and low body mass index (BMI) have been reported to be independent predictors of poor outcome in HF patients.[8–12] In contrast, it has never been studied whether delayed ambulation is associated with poor prognosis in HF patients. Furthermore, we have found no study that investigated variables that could be used to predict when HF patients who require bed rest on admission will be able to resume ambulation.

In patients with acute respiratory failure, early initiation of physical therapy can lead to early ambulation and thus shorten the stay in the intensive care unit.[13] In the present study, we examined the number of days required until

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ambulation in HF patients who were obliged to have bed rest on admission, and investigated whether delayed ambulation was associated with adverse cardiovascular events. We then identified factors related to delayed ambulation in those clinical settings.

Methods

Patients

We retrospectively studied the cases of 462 patients who were admitted to Hokkaido University Hospital for acute HF between January 2009 and December 2013. The inclusion criteria were: (1) age ≥18 years; (2) New York Heart Association (NYHA) functional class III or IV; and (3) requirement of bed rest on admission. HF was diagnosed on the basis of the Framingham criteria with either preserved or reduced ejection fraction on echocardiography according to the American College of Cardiology Foundation/American Heart Association Task Force on Practice guidelines, as determined by 2 or more cardiologists.[14,15] To minimize the confounders that could affect the ambulation period, patients were excluded if they had a restriction of ADL due to neurological or orthopedic disease or a condition for which mechanical ventilation or a circulatory device were needed. According to these inclusion and exclusion criteria, we excluded patients who were NYHA class I or II, did not require bed rest on admission (n=300), had restricted ADL (n=49), and needed mechanical devices (n=12; **Supplementary Figure 1**). A final total of 101 patients were enrolled in the present study. The protocol was approved by the Medical Ethics Committee of Hokkaido University Hospital in accordance with the ethical principles described in the Declaration of Helsinki (2013 revised version).

Definition of Ambulation Period

We determined the day that each patient achieved ambulation on the basis of their medical records. Ambulation was defined as independent walking in the hospital ward without any assistance from another person and without HF-related symptoms such as dyspnea after the stabilization of hemodynamic parameters.

Demographic and Clinical Characteristics

Using the medical records, we analyzed the patient demographic data and vital signs on admission including age, gender, BMI, heart rate, systolic blood pressure (SBP) and diastolic blood pressure, and oxygen saturation. Clinical characteristics were recorded, including the causes of HF, factors that would exacerbate HF, medical history, and prior hospitalization due to HF.

Factors that would exacerbate HF at home before admission were identified in each patient: (1) lack of adherence to self-management including diet, exercise, and medical treatment;[16] (2) arrhythmia; (3) infection; (4) uncontrolled BP (SBP ≥140 mmHg despite appropriate antihypertensive therapy on the basis of the Japanese Society of Hypertension guidelines for the management of hypertension);[17] (5) myocardial ischemia; and (6) one or more history of readmission due to HF. Geriatric nutritional risk index (GNRI), a useful parameter to evaluate nutritional status, was calculated using BMI and albumin concentration according to the modified version:[18] GNRI= 14.89×serum albumin (g/dL)+41.7×BMI/22.

Medication use before admission (angiotensin-converting enzyme inhibitor, angiotensin II receptor blocker, β-blocker, aldosterone antagonist, diuretics, and digoxin) and management on admission (inotropic agents and vasodilator agents) were also determined based on the medical records. Laboratory data including hemoglobin (Hb), albumin, blood urea nitrogen (BUN), creatinine (Cr), estimated glomerular filtration rate (eGFR), sodium (Na), potassium, and brain natriuretic peptide (BNP) were obtained upon hospital admission. Left ventricular ejection fraction (LVEF), LV end-systolic diameter (LVDs), and LV end-diastolic dimension (LVDd) were assessed on transthoracic echocardiography. Anemia was defined according to the World Health Organization criteria.[19]

Cardiovascular Events

Major adverse events, including any cardiac death or unplanned rehospitalization due to an exacerbation of HF, ventricular tachycardia or fibrillation, ischemic heart disease, and stroke, were monitored for up to 1 year after hospital discharge.

Statistical Analysis

Continuous variables are expressed as mean ± SD for normally distributed variables, and median (IQR) for non-normally distributed variables. Categorical variables are described as proportions. Baseline characteristics were compared between patients with and without major adverse events, and the variables that were significantly different were used in stepwise selection to construct a multivariate Cox proportional hazard regression model.

Adjusted hazard ratios (HR) and 95% confidence interval (CI) were calculated for each variable. Receiver operating characteristic (ROC) analysis was performed to define the optimal cut-off of time to ambulation for the prediction of cardiovascular outcomes during follow-up period. Kaplan-Meier analysis with log-rank test was performed to assess the event-free rates with respect to the combined cardiovascular events in 1 year after discharge.

To investigate the association between delayed ambulation and each clinical variable, we performed a univariate logistic regression analysis. All clinical variables that were potentially associated with delayed ambulation and had $P<0.05$ on univariate analysis, including age >65 years, lack of adherence, BUN, and eGFR, were entered into a stepwise multivariate analysis, where $P<0.1$ was used as the criterion to retain the variable. Multivariate logistic regression analysis was conducted with age, gender, and BUN, where gender was forced into the final model. All analyses were performed using JMP Pro 12.2.0 (SAS Institute, Cary, NC, USA). The differences were considered significant for $P<0.05$.

Results

The patient characteristics for the total cohort are listed in **Table 1**. Mean age was 66±17 years and 70.3% of the 101 patients were men. With regard to vital signs, lower SBP was noted compared with the prior Japanese registries for acute HF.[20] The causes of HF were dilated cardiomyopathy (DCM) in 31.7%, ischemic heart disease in 22.8%, valvular heart disease in 18.8%, and hypertensive heart disease in 16.8%. The most prevalent factor in exacerbation of HF was lack of adherence to self-management in 70.3%, and the most common comorbidity was hypertension (52.5% of the patients). Prior hospitalization due to HF was

Table 1. Patient Characteristics

	Total cohort (n=101)	Cardiovascular event (n=34)	No cardiovascular event (n=67)	P-value
Age (years)	66±17	67±19	65±16	0.674
Male	70.3	70.6	70.1	0.964
BMI (kg/m²)	24.3±4.8	24.8±5.0	24.0±4.7	0.432
Length of hospital stay (days)	40 (30–50)	43 (26–58)	39 (30–49)	0.264
Days to achieve ambulation	9 (6–17)	11 (8–20)	7 (5–15)	0.001
Causes of HF				
Ischemic	22.8	23.5	22.4	0.897
Valvular heart disease	18.8	20.6	17.9	0.745
Hypertensive heart disease	16.8	14.7	17.9	0.684
Dilated cardiomyopathy	31.7	35.3	29.9	0.578
Factors for exacerbation of HF				
Lack of adherence to self-management	70.3	32.4	67.6	0.818
Arrhythmia	11.9	16.7	83.3	0.329
Infection	9.9	70.0	30.0	0.029
Uncontrolled BP	4.9	40.0	60.0	0.758
Myocardial ischemia	3.0	0.0	100.0	0.549
Medical history				
Hypertension	52.5	64.7	46.3	0.080
Diabetes mellitus	38.6	38.2	38.8	0.956
Atrial fibrillation	47.5	50.0	46.3	0.723
Sustained VT/VF	16.8	14.7	17.9	0.684
Prior hospitalization due to HF	57.4	79.4	46.3	0.002
Vital signs				
Heart rate (beats/min)	84±23	84±21	84±25	0.960
SBP (mmHg)	124±29	121±31	125±28	0.499
DBP (mmHg)	73±22	72±21	74±23	0.603
Oxygen saturation (%)	98±1	98±1	98±1	0.938
NYHA functional class				
III	64.4	70.6	61.2	0.352
IV	35.6	29.4	38.8	0.352
GNRI	97.8±11.7	96.4±11.7	98.5±11.6	0.387
Laboratory data				
Hemoglobin (g/dL)	12.0±2.5	11.7±2.1	12.2±2.6	0.281
Serum albumin (g/dL)	3.5±0.5	3.3±0.6	3.6±0.5	0.033
BUN (mg/dL)	21 (16–36)	25 (19–41)	20 (15–29)	0.192
Serum creatinine (mg/dL)	1.32±0.99	1.47±0.78	1.25±1.08	0.291
eGFR (mL/min/1.73 m²)	51.6 (35.5–68.7)	47.7 (25.2–62.0)	54.1 (40.6–76.8)	0.029
Sodium (mEq/L)	138±5	136±5	139±4	0.032
Potassium (mEq/L)	4.3±0.5	4.3±0.5	4.3±0.5	0.700
Plasma BNP (pg/mL)	627 (305–1,282)	901 (406–1,655)	541 (265–1,045)	0.204
LVEF (%)	36±18	36±18	36±17	0.933
LVDd (mm)	58.4±11.5	59.0±13.5	58.1±10.4	0.718
LVDs (mm)	47.4±14.3	48.0±16.7	47.1±13.1	0.753
Medication use before hospitalization				
ACEI	28.7	32.4	26.9	0.565
ARB	32.7	41.2	28.4	0.194
β-blocker	52.5	52.9	52.2	0.947
Aldosterone antagonist	32.7	41.2	28.4	0.194
Diuretics	69.3	82.4	62.7	0.043
Digitalis	19.8	25.0	75.0	0.436
I.v. medication use before hospitalization				
Inotropic agents	23.8	29.4	20.9	0.342
Vasodilators	57.4	50.0	61.2	0.282
Furosemide	67.3	64.7	68.7	0.823

Data given as %, mean ± SD or median (IQR). ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; BMI, body mass index; BNP, brain natriuretic peptide; BUN, blood urea nitrogen; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; GNRI, Geriatric Nutritional Risk Index; HF, heart failure; LVDd, left ventricular end-diastolic diameter; LVDs, left ventricular end-systolic diameter; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; SBP, systolic blood pressure; VT/VF, ventricular tachycardia/fibrillation.

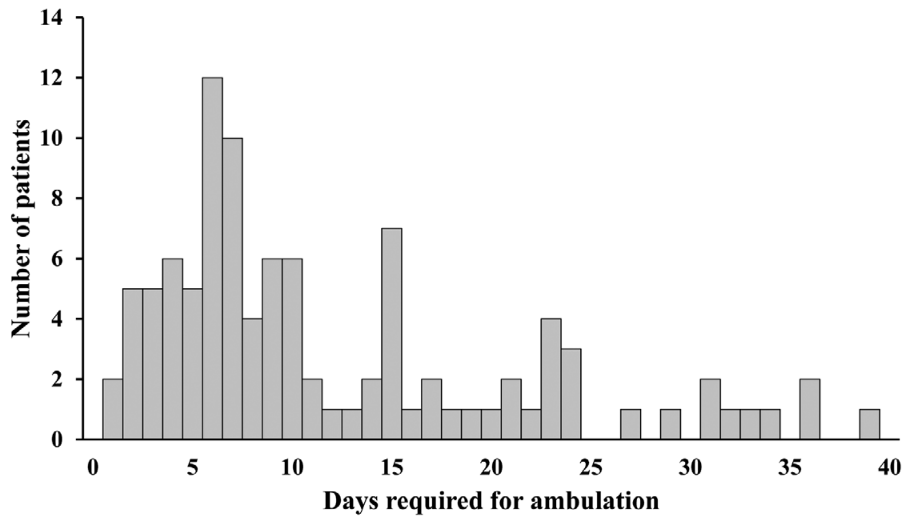

Figure 1. Distribution of the number of days required to achieve ambulation in patients with heart failure (n=101).

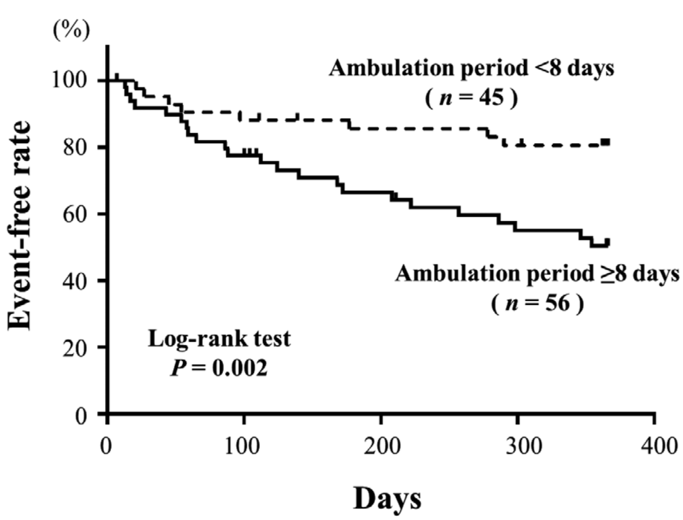

Figure 2. Kaplan-Meier event-free rate from any cardiac death and rehospitalization due to worsening heart failure, ventricular tachycardia or fibrillation, ischemic heart disease, and stroke in heart failure patients according to presence of delayed ambulation. The cut-off of the ambulation period of 8 days was determined on receiver operating characteristic curve analysis. The significance of separation between the 2 groups was examined using log-rank test during a mean follow-up of 244±15 days.

identified in 57.4%.

As for the short-term prognosis, the length of hospital stay was longer in patients with delayed ambulation than in those with early ambulation (45 days vs. 34 days, P=0.003). In contrast, there was no significant difference in mortality or HF rehospitalization rate ≤30 days after discharge between the 2 groups (10.7% vs. 4.4%, P=0.293). There were no in-hospital deaths. During the mean follow-up of 244±15 days, there were 34 (33.7%) cardiovascular events, consisting of 10 cardiac deaths and 24 unplanned rehospitalization. Of these, the rehospitalization cause was worsening HF in 14 patients, ventricular tachycardia or fibrillation in 5 patients, ischemic heart disease in 4 patients, and cerebrovascular events in 1 patient. When the patients were divided into 2 groups according to the presence or absence of cardiovascular events, the mean age, gender, BMI, and causes of HF were similar between the 2 groups. Patients with cardiovascular events had longer days to acquire ambulation (P=0.001) than event-free patients. Infection as the precipitating factor and prior hospitalization due to HF were also more frequently observed in the cardiovascular event group. Lower serum albumin, eGFR, and sodium concentration were evident in patients with adverse outcomes. As for nutritional status, GNRI was similar between the 2 groups, and there was no significant difference in Hb or BNP concentration, or in LVEF between patients with or without cardiovascular events.

The distribution of the days required to achieve ambulation in the total cohort of patients is shown in **Figure 1**. The median period was 9 days (IQR, 6–17 days), and on ROC analysis, ambulation period 8 days was identified as the optimal cut-off for discriminating adverse outcomes (**Supplementary Figure 2**). Area under the curve (AUC) for

Table 2. Multivariate Cox Proportional Hazard Analysis for Cardiac Death and HF-Related Rehospitalization

	HR	95% CI	P-value
Age	0.99	0.97–1.01	0.387
Male	1.15	0.57–2.54	0.707
Time to achieve ambulation ≥8 days	3.13	1.44–7.59	0.003
Prior hospitalization for HF	3.50	1.58–8.84	0.002

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

Table 3. Univariate Predictors of Delayed Ambulation in HF Patients

	OR	95% CI	P-value
Age >65 years	2.61	1.15–6.11	0.022
Male	0.93	0.39–2.20	0.872
BMI (per 1-kg/m^2 increase)	1.07	0.98–1.17	0.143
Factors for exacerbation of HF			
Lack of adherence to self-management	2.44	1.03–5.98	0.042
Arrhythmia	0.53	0.15–1.79	0.308
Infection	1.23	0.33–5.08	0.759
Uncontrolled blood pressure	0.19	0.01–1.32	0.096
Prior hospitalization due to HF	1.88	0.85–4.23	0.120
NYHA functional class IV	1.72	0.75–4.03	0.202
GNRI (per 1-unit decrease)	0.99	0.97–1.03	0.965
Anemia†	1.58	0.71–3.54	0.265
Serum albumin (per 1-g/dL decrease)	0.52	0.23–1.11	0.091
BUN (per 1-mg/dL increase)	1.04	1.02–1.08	<0.001
eGFR <60 mL/min/1.73 m^2	2.86	1.26–6.68	0.012
Sodium (per 1-mEq/L decrease)	0.95	0.87–1.03	0.248
Potassium (per 1-mEq/L increase)	1.34	0.64–2.92	0.439
Log BNP (per 1-pg/mL increase)	1.37	0.96–1.99	0.081
LVEF <40%	1.13	0.51–2.52	0.765
LVDd (per 1-mm increase)	1.01	0.97–1.04	0.747
Medication			
ACEI	1.46	0.61–3.61	0.393
ARB	1.65	0.71–3.96	0.246
β-blocker	1.10	0.50–2.43	0.806
Aldosterone antagonist	0.95	0.41–2.20	0.899
Diuretics	1.82	0.78–4.33	0.167
Digitalis	0.59	0.22–1.58	0.295
Inotropic agents	1.85	0.72–5.04	0.201
Vasodilators	1.59	0.72–3.56	0.250
Furosemide	0.95	0.41–2.19	0.899

†Hemoglobin <13 g/dL (male) or <12 g/dL (female). Abbreviations as in Tables 1,2.

the prediction of cardiovascular events was 0.66 with 77% sensitivity and 55% specificity. Adverse events occurred more frequently in patients with the longer ambulation period (≥8 days) compared with those with the shorter period (<8 days; 46.4% vs. 17.8%, P=0.002; **Figure 2**). Of the adverse events, the number of cardiac deaths was similar between the groups (longer vs. shorter, 7 vs. 3, P=0.067), while number of rehospitalizations due to HF was higher in patients with the longer ambulation period than in those with the shorter period (14 vs. 0, P=0.007).

Clinical variables that differed significantly (P<0.05) according to cardiovascular event status (**Table 1**) were entered into stepwise selection to construct a multivariate Cox proportional hazard regression model. This included longer ambulation period (≥8 days), infection as a precipitating factor, prior history of HF, serum albumin, Na, eGFR, as well as age and gender, which were forced into the final model. As shown in **Table 2**, longer ambulation period and prior hospitalization due to HF were independent predictors of cardiac events in patients with HF. In contrast, the ambulation period as a continuous variable was not an independent predictor in multivariate analysis (HR, 1.03; 95% CI: 0.99–1.07).

To clarify the factors related to delayed ambulation, univariate (**Table 2**) and multivariate logistic regression analyses were conducted (**Table 3**). On univariate analysis, age >65 years, lack of adherence to self-management, BUN, and eGFR <60 mL/min/1.73 m^2 were significantly associated with delayed ambulation. Causes of HF, comorbidities, and vital signs including heart rate and BP were

Table 4. Multivariate Predictors of Delayed Ambulation

	OR	95% CI	P-value
Age >65 years	2.49	1.04–6.09	0.039
Male	1.07	0.42–2.77	0.878
BUN	1.04	1.01–1.08	0.002

Abbreviations as in Tables 1,2.

not significantly associated with delayed ambulation (data not shown). On multivariate analysis, age >65 years and increased BUN were independent predictors of delayed ambulation (**Table 4**).

Discussion

The present analysis of 101 hospitalized patients with HF who required bed rest on admission has shown that patients with cardiovascular events had longer days to acquire ambulation than those without cardiovascular events. The period until ambulation to discriminate the adverse outcomes was 8 days, and the delayed ambulation period (≥8 days) together with prior hospitalization for HF, was an independent determinant for cardiovascular events. In addition, older age (>65 years) and higher BUN were identified as independent predictors of delayed ambulation. Although early ambulation is associated with the better prognosis in patients hospitalized with HF,[21] this is the first report to clarify the negative impact of delayed ambulation on clinical outcomes in Japanese patients with HF.

We retrospectively analyzed HF patients at a single center in Japan, and the characteristics of the patients (i.e., age, BMI, comorbidity, and medication use) were similar to those in the Japanese Cardiac Registry of Heart Failure in Cardiology (JCARE-CARD).[22] The prevalence of DCM was relatively high due, in part, to the selection bias given that this study was conducted at a single center of a university hospital. In addition, SBP at admission in the present study was lower compared with a report from the national consortium of acute HF registries,[20] potentially due to the younger age, lower prevalence of hypertension, and higher percentage of DCM with lower LVEF. Nevertheless, the present findings appear to reflect the real-world scenario in Japan. In the present study, 9 days was the median period required for ambulation in patients with acute HF. Delayed ambulation may lead to prolonged hospital stay, and in the present study, the median period of hospitalization was 40 days (data not shown). Median length of hospital stay was 15 days in the JCARE-CARD population,[23] and 21 days in the Acute Decompensated Heart Failure Syndromes (ATTEND) registry.[24] The present length of hospital stay was longer than those in the prior HF registries.[20] This could be due to the fact that HF patients with mild HF (NYHA I or II) were completely excluded in this study and that the proportion of patients with cardiomyopathy (in whom the optimal β-blocker dose is not immediately clear) was relatively high. Overall, in Japan, not only the length of hospital stay but also the period required for ambulation is much longer than in Western registries.[6,7]

The longer period of hospitalization in Japan can be explained by the differences in the health-care system and the continued treatment for comorbidities, as well as the intensive management of risk factors during the hospitalization for worsening HF. Indeed, it has been reported that the length of hospital stay is not associated with all-cause mortality after discharge,[25,26] which also suggests that the length of hospital stay is not necessarily affected by the pathogenesis, severity, or treatment of HF. The period required for ambulation after admission to hospital, however, appears not to be associated with the social factors such as the health-care system. Instead, the period for ambulation is more closely related to the severity and prognosis of HF. Interestingly, the ambulation period seemed not to be influenced by the mechanisms of exacerbation of HF because the prevalence of clinical scenario indicating central volume shift or fluid retention did not differ between patients with delayed ambulation and those with early ambulation (data not shown).

As expected, delayed ambulation (≥8 days) was associated with longer hospital stay and adverse cardiac events during 8-month follow-up, even after adjustment for confounding factors. Prolonged bed rest as a result of delayed ambulation is likely to lead to physical deconditioning and a further reduction in ADL.[27] Specifically, skeletal muscle strength and mass are decreased in patients with HF,[2,3] and these decreases rapidly progress when a patient is on bed rest.[28,29] Short-term immobilization (only 3 days) has been shown to induce a 10% reduction in skeletal muscle mass.[30] Given that muscle atrophy is an independent predictor of exercise capacity and long-term outcome in HF,[31] muscle deconditioning in the acute phase may potentially affect long-term prognosis. Thus, delayed ambulation is thought to form a vicious circle that causes further long-term bed rest through skeletal muscle atrophy. Although skeletal muscle mass was not evaluated in this study, the worse prognosis, particularly the higher rate of HF rehospitalization, in patients with delayed ambulation may be attributed to reduced exercise capacity due to their deconditioned state.

Unfortunately, due to the retrospective manner of this study, the cause-and-effect relationship between delayed ambulation and prognosis was difficult to determine. In addition, the confounders that hamper walking, such as patient frailty, cannot be completely excluded. Early mobilization and exercise therapy in critically ill patients in an intensive care unit, however, have been shown to be associated with better clinical outcomes, such as the prevention of delirium.[32] Furthermore, a progressive mobilization program has been shown to reduce hospital stay and improve early clinical outcomes in patients with acute HF.[33] This suggests that the delayed ambulation per se may be a therapeutic target for patients hospitalized for worsening HF, and underscores the importance of providing early ambulation and physical therapy to those with a high risk of delayed ambulation.

In the present analysis, older age (>65 years) was an independent predictor of delayed ambulation. In contrast, age-related decline in skeletal muscle function is attributable to not only physical inactivity but also to intrinsic skeletal muscle mitochondrial dysfunction.[34,35] In addition, recovery of skeletal muscle mass after immobilization is slower in old than young subjects.[36] Taken together, age may be related to progressive impairment of skeletal muscle function during bed rest, and to slower recovery of skeletal muscle mass after immobilization, resulting in the delayed ambulation in old HF patients.

Increased BUN was found to be an independent predictor of delayed ambulation in the present study. Renal dysfunction is a frequent complication in HF patients, and it is an independent predictor of death or cardiac events.[37] In a JCARE-CARD study, decreased eGFR at discharge was shown to worsen the prognosis of HF patients.[9] Worsening renal failure, defined as an increase in serum Cr, during the treatment of HF is closely associated with cardiac events during hospitalization.[38] Serum BUN on admission is also associated with in-hospital mortality of HF patients.[39,40] In the present study renal dysfunction was an important factor in delayed ambulation, as well as in the prognosis of HF patients. Renal dysfunction often makes it difficult to manage the fluid balance in HF patients, which may result in delayed recovery to compensated HF. BUN is also increased as a result of the body's enhanced catabolism,[41] which is associated with cardiac cachexia in patients with HF. BUN may therefore be associated with delayed ambulation as a factor of enhanced catabolism.

Study Limitations

There are several limitations to be addressed. First, this study was a retrospective observation at a single center. We were unable to address the involvement of potential factors that were not included in the patients' medical records. In particular, there were no data on muscle amount or strength, which could well be associated with ADL and the ambulation period. Further studies evaluating ADL before admission may shed light on this issue. Second, we divided the patients into 2 groups based on a time to ambulation of 8 days, which can discriminate adverse cardiac events. Further prospective studies are needed to confirm the clinical validity of this cut-off value. Third, we cannot rule out the possibility that the difference in educational intervention during this period will affect long-term prognosis, because the length of hospitalization differs in the presence or absence of delayed ambulation. Finally, we excluded patients who had restricted ADL due to neurological or orthopedic disease, but the majority of older HF patients have these comorbidities, and their ADL are reduced in general. Further studies with HF subjects who have these comorbidities are necessary.

Conclusions

We have, for the first time, shown that delayed ambulation is associated with poor prognosis in patients with acute HF and that older age and increased BUN are independent predictors of delayed ambulation. To accomplish early ambulation and prevent delayed ambulation, early initiation and long-term continuation of comprehensive cardiac rehabilitation are needed in order to shorten bed-rest period and improve physical function, leading to reduction of cardiac deaths and HF rehospitalizations in this vulnerable population.

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Disclosures

The authors declare no conflicts of interest.

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Supplementary Files

Please find supplementary file(s);
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