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ORIGINAL ARTICLE
Cardiac Rehabilitation

Progressive Mobilization Program for Patients With Acute Heart Failure Reduces Hospital Stay and Improves Clinical Outcome

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Background: Early ambulation has been shown to be associated with shorter hospital stay and better clinical outcomes in patients with acute heart failure (HF). Early mobilization program in combination with structured exercise training is recommended, but has yet to be developed and implemented in HF.

Methods and Results: We developed a progressive mobilization program for HF patients that classifies the mobilization process into 7 stages based on disease condition and physical function. We retrospectively analyzed 136 patients with acute HF (80±11 years), who were assigned either to the mobilization program (intervention group, n=75) or to usual care (control group, n=61). The program was safely implemented without any adverse events. Hospital stay was significantly reduced in the intervention group compared with the control group (33±25 vs. 51±36 days, P<0.01). The intervention group had higher activities of daily living (ADL) score at discharge evaluated using the Barthel index (64±38 vs. 49±36, P<0.05). The intervention group also had a higher percentage of discharge to home (71% vs. 52%, P<0.05) and a lower rate of HF-related readmission (16% vs. 36%, P<0.05) compared with the control group.

Conclusions: The progressive mobilization program for acute HF was feasible and was associated with better ADL and reduced hospital stay, leading to improvement of clinical outcome.

Key Words: Activity of daily living; Acute heart failure; Cardiac rehabilitation; Early ambulation; Mobilization program

With the increase in life expectancy worldwide over the last decade, the number of patients with heart failure (HF) is dramatically increasing; a phenomenon called "the HF pandemic".[1] Elderly HF patients often have multiple comorbidities such as anemia, cognitive impairment, and skeletal muscle atrophy (sarcopenia), all of which contribute to limit activities of daily living (ADL).[2–5] When such patients are hospitalized with acute HF, restricted mobilization and prolonged bed rest for the treatment or due to the congestive symptoms are likely to cause physical deconditioning, which leads to further impairment in ADL.[6] Indeed, according to recent large-scale registry data, early ambulation of HF patients is associated with a reduction in the length of hospital stay and HF readmission rate.[7] Thus, minimizing the length of hospital stay is encouraged in the clinical guidelines for the treatment of acute HF.[8,9] One promising intervention for this purpose is a mobilization program during the early stage of HF.

Progressive mobilization programs in patients with stroke or acute respiratory failure, and in critically ill patients in an intensive care unit (ICU) have been shown to be associated with better clinical outcomes, such as the prevention of delirium.[10–12] In the setting of HF, it is also imperative to ensure hemodynamic stabilization and the relief of congestion in the process of early mobilization in order to prevent the in-hospital worsening of HF.[13] This includes daily monitoring of weight, vital signs such as orthostatic blood pressure, and subjective symptoms, as well as the onset of arrhythmia, and daily monitoring of laboratory data, and chest X-ray.[9,14] In addition, the hospitalization phase of acute HF is an opportunity to

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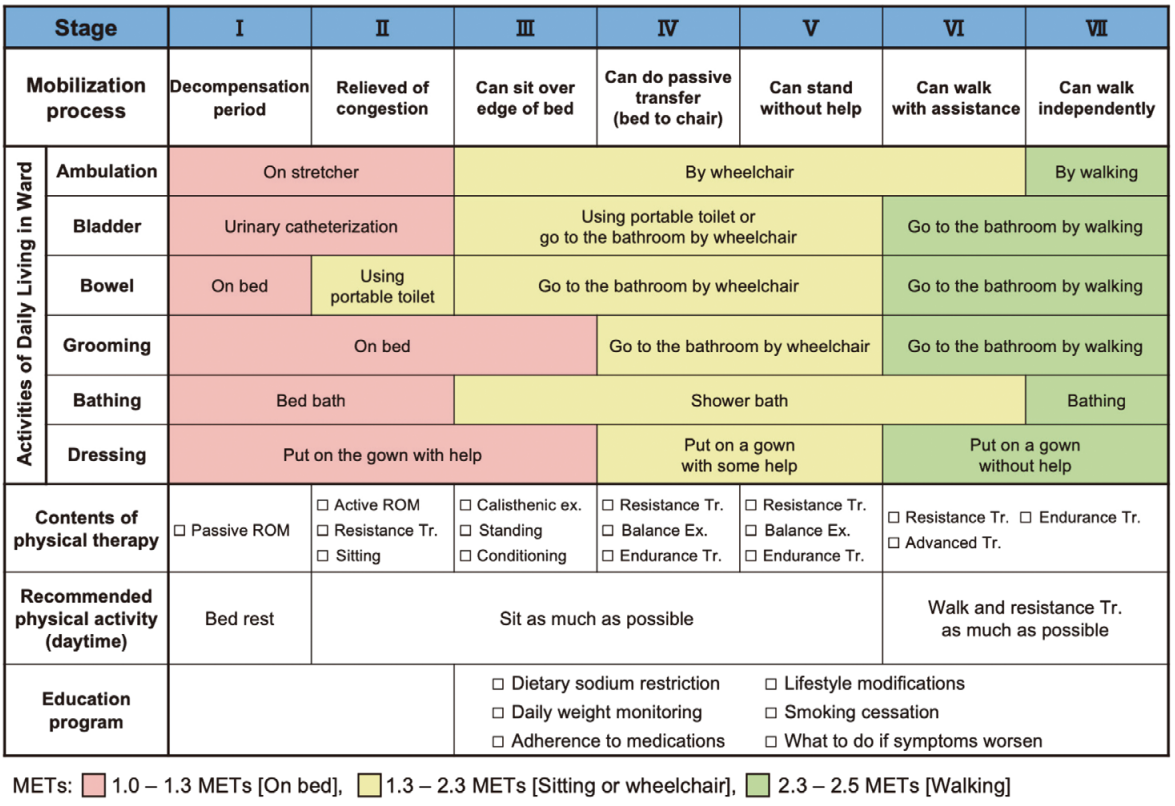

Figure 1. Staged mobilization program for patients with acute heart failure developed on the basis of patient condition and possible mobility in a general ward with corresponding metabolic equivalents (MET). ROM, range of motion.

provide tailored exercise training according to individual physical conditions and to ensure education for self-care monitoring.[9,14] Accordingly, a progressive and integrated mobilization program introduced by a multidisciplinary HF team based on objective indices could provide early initiation of physical therapy and efficient management for HF, potentially leading to shorter hospital stay and improvement in early prognosis. Although exercise has been shown to improve the functional outcome in stable HF patients,[15,16] a progressive mobilization program targeting the acute phase of HF has yet to be developed, and its clinical significance remains unclear.

The present study was therefore conducted to determine (1) whether a progressive mobilization program is feasible and safe in HF patients; and (2) the effects of this program on physical function, discharge disposition, and clinical outcome.

Methods

Patients

This was a single-center and retrospective study, designed to determine the feasibility of a mobilization program and its potential safety and efficacy, in order to provide an estimate of the intervention effect size in future clinical trials. We included all consecutive patients who were hemodynamically stabilized after the introduction of i.v. medication for acute HF, that is, de novo or worsening HF, in the cardiovascular department of Hokkaido Social Work Association Obihiro Hospital from January 2009 to May 2015. During the study period, the eligible patients admitted from July 2013 to May 2015 were assigned to the intervention group using a progressive mobilization program, and those admitted from January 2009 to June 2013 were allocated to the control group receiving usual care. On the basis of Framingham criteria, HF with preserved ejection fraction (HFpEF) or HF with reduced ejection fraction on echocardiography was diagnosed according to the American College of Cardiology Foundation/American Heart Association Task Force on Practice guidelines, as determined by 2 or more cardiologists.[14] The inclusion criterion was age ≥20 years. We excluded patients requiring mechanical ventilation or circulatory support. This study was approved by the Medical Ethics Committee of Hokkaido Social Work Association Obihiro Hospital in accordance with the Declaration of Helsinki (2013 revised version), and informed consent was obtained from all of the patients.

Development of the Progressive Mobilization Program

The progressive mobilization program was developed with the involvement of a multidisciplinary HF team that included nurses, physical therapists, and cardiologists. This program classifies the mobilization process into 7 stages based on disease condition (decompensated or compensated) and possible mobility in the general ward (i.e., sitting over the edge of the bed; passively transferring from the

Table 1. Criteria for Change in Progressive Mobilization Program Stage in HF

(A) The criteria to increase the stage require confirmation that there are none of the following findings during physical therapy:
• Insufficient mobility function required at the next stage
• ≥20-mmHg decrease in SBP and/or ≥10 mmHg in DBP (postural hypotension)
• ≥30-beats/min increase in heart rate
• >4% decrease in SpO_2
• Symptoms: angina, palpitations, dizziness, nausea, fatigue, and dyspnea with ≥14 on the Borg Rating of Perceived Exertion Scale (6–20)
(B) The criteria to decrease the stage require 1 major or ≥2 minor criteria.
Major criteria:
• Falling down or related injuries on the ward
• Heart rate at rest <40 beats/min or >130 beats/min
• New onset of arrhythmias
• Any increase in plasma BNP or NT-proBNP compared with the previous value
• Larger cardiothoracic ratio than the last ratio on chest X-ray
• >1.8-kg increase in body weight over the previous 1–3 days
Minor criteria:
• Worsening of fatigue, edema, or dyspnea
• >10-beats/min increase in heart rate over 1–3 days
• Significant decrease in urine output

BNP, brain natriuretic peptide; DBP, diastolic blood pressure; HF, heart failure; NT-proBNP, N-terminal prohormone of brain natriuretic peptide; SBP, systolic blood pressure; SpO_2, oxygen saturation of peripheral artery.

bed to a chair; standing without help; walking with assistance; and walking independently), according to an ICU mobility scale with some modifications.[17]

The ADL, that is, physical ambulation; bladder emptying; bowel emptying; grooming; bathing; and dressing; were grouped according to the corresponding metabolic equivalents (MET; **Figure 1**) in the stages of the mobilization program. For instance, urinary catheterization (stages I,II) referred to 1.0 MET; using portable toilet (stages III–V) to 1.3 MET, going to the bathroom by wheelchair (stages III–V) to 1.3 MET; or going to the bathroom by walking (stages VI,VII) to 2.3 MET. The objective criteria to increase or decrease each stage of the mobilization program, based on a consensus statement for cardiac rehabilitation, are listed in **Table 1**.[8] When increasing the stage, none of the following can be present: insufficient mobility function required at the next stage; ≥20-mmHg decrease in systolic blood pressure and/or ≥10 mmHg in diastolic pressure; ≥30-beats/min increase in heart rate (HR); >4% decrease in oxygen saturation (SpO_2); and exacerbation of symptoms ≥14 on the Borg Rating of Perceived Exertion Scale (RPE; 6–20). When decreasing the stages, the patients had to meet one of the major criteria or ≥2 of the minor criteria. The major criteria were: falling down or related injuries on the ward; HR at rest <40 beats/min or >130 beats/min; new onset of arrhythmia; any increase in plasma N-terminal pro-brain natriuretic peptide (NT-proBNP) compared with the previous value; a larger cardiothoracic ratio than the previous ratio on chest X-ray; and >1.8 kg increase in body weight (BW) over the previous 1–3 days. The minor criteria were: worsening of fatigue, edema, or dyspnea; >10-beats/min increase in HR over 1–3 days; and significant decrease in urine output. These parameters were assessed and the stage modification was conducted by physical therapists, nurses, and one or more cardiologists.

Program Implementation

All hospitalized subjects (stage I) were first ascertained as having compensated HF without acute coronary syndrome, cardiogenic shock, myocarditis, or malignant arrhythmia. The treating physicians then gave a prescription to physical therapists and nurses to implement the progressive mobilization program for the eligible patients. On the basis of mobility function and hemodynamics, the physical therapist applied the optimal first stage as stage I up to stage VII. Physical therapy interventions focused on the mobility function required for the next stage are shown in **Supplementary Figure**. In stage I, the therapist carefully administered a passive range of motion (ROM) exercise for the lower and upper extremities at bedside to prevent contracture. In stage II, manual resistance training together with active ROM exercise were performed at 3–5 repetitions for the purpose of improving trunk muscle strength for sitting balance. From stage III, calisthenic exercise, a variety of simple movements using one's own body for resistance, was initiated at 5–10 repetitions with very low intensity (<30% of 1-repetition maximum [RM]) to increase body strength and flexibility for the passive transfer.

In stages IV and V, endurance training was conducted along with frequent resistance training at mild intensity (30–40% of 1-RM) to improve standing balance and endurance for the achievement of gait ability. In stages VI and VII, an aerobic exercise using an ergometer or walking was conducted with moderate-intensity resistance training (40–60% of 1-RM) to improve exercise tolerance and muscle strength, which are required for ADL after discharge. Other staff including nurses and nursing assistants proceeded to increase the patient's physical function on the ward according to the ADL chart and optimal MET in the mobilization program.

From stage III or more, multidisciplinary staff (i.e., dieticians, physical therapists, pharmacists, nurses, and physicians), provided the patient with education that included information on dietary sodium restriction, lifestyle modifications, daily weight monitoring, smoking cessation, adherence to medication, and symptom management.[18]

Table 2. HF Patient Characteristics

	Control group	Intervention group	P-value
n	61	75	
Age (years)	81±11	79±11	0.423
Male	17 (28)	35 (47)	0.033
BMI (kg/m²)	22.2±4.5	22.8±5.0	0.504
Vital signs			
Heart rate (beats/min)	75±13	72±11	0.522
SBP (mmHg)	116±14	118±11	0.677
DBP (mmHg)	68±10	66±11	0.660
NYHA class (II/III/IV)	39/15/7	52/16/7	0.797
Etiology of HF			
Ischemic heart disease	13 (21)	19 (25)	0.686
HTD	22 (36)	23 (31)	0.584
DCM	0 (0)	6 (8)	0.033
Valvular heart disease	9 (15)	9 (12)	0.800
Others	17 (28)	18 (24)	0.608
HFpEF	36 (68)	49 (66)	0.840
Medical history			
Hypertension	34 (56)	45 (60)	0.616
Diabetes	17 (28)	24 (32)	0.708
Chronic kidney disease	14 (23)	12 (16)	0.382
COPD	3 (5)	5 (7)	0.731
Atrial fibrillation	27 (44)	33 (44)	0.976
Stroke	17 (28)	14 (19)	0.223
Dementia	7 (11)	14 (19)	0.341
Prior hospitalization due to HF	36 (59)	34 (45)	0.124
Laboratory data			
Hemoglobin (g/dL)	11.0±2.0	11.4±2.0	0.249
Total protein (g/dL)	6.2±0.7	6.1±0.7	0.871
Serum albumin (g/dL)	3.2±0.5	3.3±0.6	0.641
Serum sodium (mEq/L)	139±4	140±4	0.080
BUN (mg/dL)	31.9±20.6	25.9±15.8	0.059
Serum creatinine (mg/dL)	1.45±1.32	1.28±1.40	0.465
eGFR (mL/min/1.73 m²)	49.4±30.8	53.4±30.3	0.442
NT-proBNP (pg/mL)	2,098 (1,070–4,688)	1,597 (476–4,115)	0.960
LVEF (%)	55±13	54±13	0.740
Medication			
ACEI or ARB	11 (18)	24 (32)	0.076
β-blocker	20 (33)	35 (47)	0.113
Diuretics	50 (82)	49 (66)	0.051

Data given as mean±SD, median (IQR), or n (%). ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blockers; BMI, body mass index; BUN, blood urea nitrogen; COPD, chronic obstructive pulmonary disease; DCM, dilated cardiomyopathy; eGFR, estimated glomerular filtration rate; HFpEF, heart failure with preserved ejection fraction; HTD, hypertensive heart disease; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association. Other abbreviations as in Table 1.

Usual Care

The control group was provided with conventional care, in which the patients were assessed comprehensively and their care plans were designed by a multidisciplinary team. Physical therapists initiated the interventions to practice safe mobility in the ward and enhance balance and muscle strength after the HF was compensated. Other pharmacological and non-pharmacological treatments, as well as patient education without using a check list, were carried out similarly to the intervention group.

Other Clinical Variables and Outcomes

We reviewed all patient medical records to evaluate demographic data including age, gender, body mass index (BMI), causes of HF, medication, and comorbidities. Echocardiography and blood sampling were performed ≤30 days before discharge. Left ventricular ejection fraction (LVEF) was calculated using the modified Simpson method on echocardiography. All patients underwent measurement of estimated glomerular filtration rate, hemoglobin, and plasma NT-proBNP. The adverse events and complications associated with the progressive mobilization program were

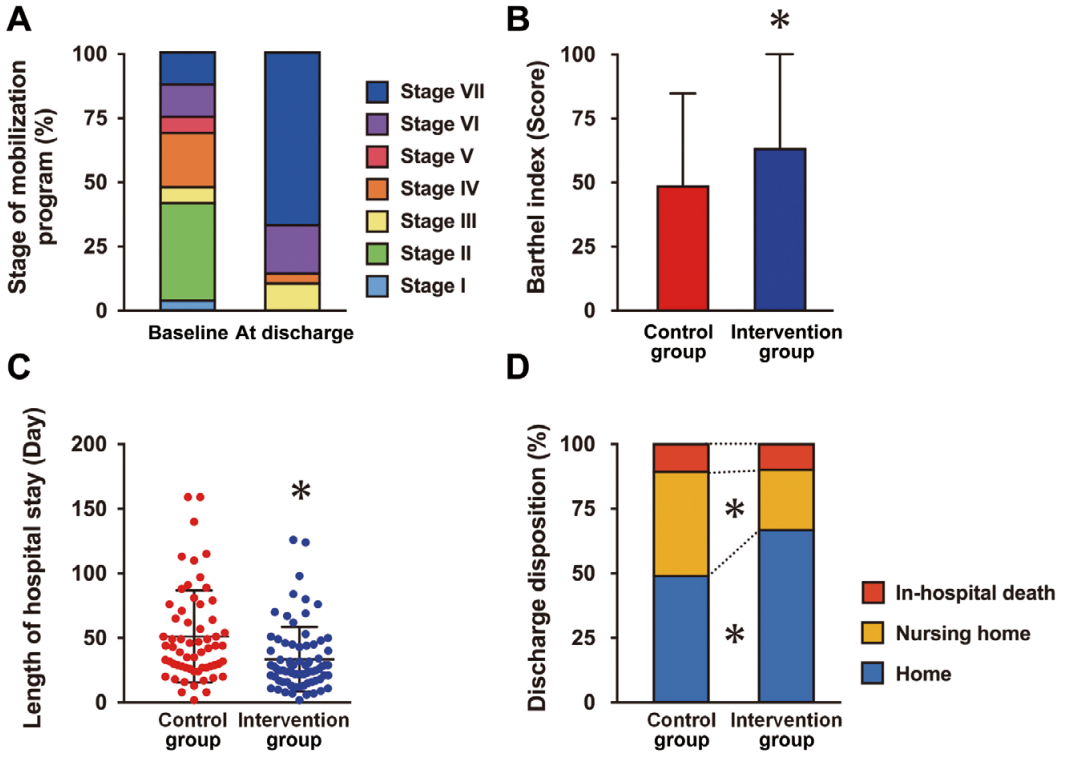

Figure 2. (**A**) Change in mobilization program stage by discharge in the progressive mobilization group. (**B**–**D**) Comparison of (**B**) Barthel index, (**C**) length of hospital stay, and (**D**) discharge disposition between the progressive mobilization group and the usual care group.

retrospectively reviewed. Patients were followed up for readmission due to worsening HF via medical chart review for up to 1 year or to the event. Patient falls and worsening HF related to overactivity were applied for the assessment of protocol safety. The primary outcome was length of hospital stay. Secondary outcomes were the discharge disposition, including in-hospital death and discharge to home or a nursing home, HF-related readmission rate after discharge, and Barthel index at discharge (evaluating 10 different abilities of ADL on a score from 0 to 100).

Statistical Analysis

We used the unpaired Student's t-test or Mann-Whitney U-test to compare continuous variables, summarized as mean±SD or median (IQR) due to a non-normal distribution, as appropriate. Categorical variables are presented as numbers or percentages and were compared using chi-squared test. We conducted Kaplan-Meier analysis with log-rank test to compare the rates of readmission due to worsening HF between the intervention group and the control group. All analyses were performed using JMP 13.1 (SAS Institute, Cary, NC, USA) and $P<0.05$ was considered significant.

Results

Patient Characteristics

A total of 136 patients were enrolled in the study. The baseline patient characteristics are listed in **Table 2**. Mean age (81±11 vs. 79±11 years) and BMI (22.2±4.5 vs. 22.8±5.0 kg/m^2) as well as vital signs and medical history were similar between the control and intervention groups. The percentage of male patients was higher in the intervention group than in the control group. The severity of HF was not different between the 2 groups, as indicated by the similar LVEF and plasma NT-proBNP level. The intervention group had a significantly higher percentage of dilated cardiomyopathy compared with the control group. The percentage of HFpEF (68% vs. 66%) was relatively high in the present study and was well balanced between the 2 groups. In addition, there was no significant difference in hemoglobin, total protein and albumin, or renal function between the groups. Serum sodium concentration tended to be higher and the blood urea nitrogen level lower in the intervention group, consistent with the relatively low percentage of diuretics use in the intervention group compared with the control group. The prescription rate of renin-angiotensin system (RAS) inhibitors and β-blockers seemed to be higher in the intervention group than the control group, but the difference was not significant.

Mobilization Program Implementation

With the implementation of the progressive mobilization program, there was no exacerbation of adverse events including falls or worsening of HF related to overactivity. The stages of the mobilization program that the participants achieved from baseline to discharge are shown in **Figure 2A**. Although 69% of the patients were unable to stand without

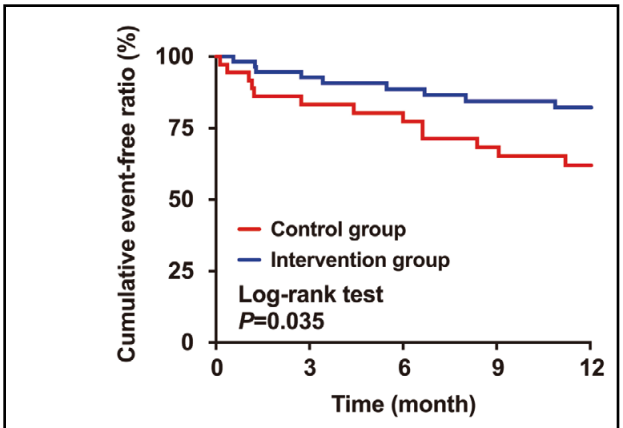

Figure 3. Kaplan-Meier curve for heart failure-related readmission in the progressive mobilization (intervention) group and the usual care (control) group.

any help at baseline (stage IV or lower), 85% of the patients were able to walk independently at discharge (stage VI or higher).

The time to initiation of physical therapy was significantly shorter in the intervention group than in the control group (6±8 vs. 15±15 days, P<0.01). In contrast, the treatment period by a physical therapist tended to be shorter in the intervention group (26±24 vs. 35±29 days, P=0.06). Notably, the intervention group acquired significantly better ADL according to Barthel index, compared with the control group (score 64±38 vs. 49±36, P<0.05; **Figure 2B**).

Length of Hospital Stay and Clinical Outcome

The HF patients in the intervention group had a significantly shorter length of hospital stay than the control group (33±25 vs. 51±36 days, P<0.01; **Figure 2C**). Of note, the mobilization program significantly affected the discharge disposition, in that more patients in the intervention group were able to be discharged home instead of to a nursing home, compared with the controls (71% vs. 52%; **Figure 2D**).

Regarding in-hospital mortality, there was no significant difference between the groups (9% vs. 10%, P=0.92; **Figure 2D**). During a median follow-up of 365 days (range, 174–365 days), readmission due to worsening HF occurred in 22 patients (24%). On Kaplan-Meier analysis the intervention group had a significantly lower risk of HF readmission compared with the control group (16% vs. 36%, P<0.05; **Figure 3**).

Discussion

The implementation of the progressive mobilization program for HF patients enabled safe achievement of early intervention by a physical therapist, resulting in a better level of ADL at discharge. Importantly, the introduction of this program enhanced the rate of home discharge, with a lower risk of HF rehospitalization during the 1 year after discharge. To our knowledge, this is the first study to develop a mobilization program for acute HF and confirm its clinical relevance.

This progressive mobilization program is characterized by 7 distinct stages based on physical activity under the supervision of a multidisciplinary HF team. In addition, the stage modification was determined using not only HF-related symptoms but also several objective parameters including vital signs, BW, plasma NT-proBNP, and cardiothoracic ratio. The staging of this program includes criteria used in the ICU mobility scale, in which the 11 stages are stratified based on activity levels that can be reasonably achieved by multidisciplinary intervention across the spectrum of recovery in an ICU.[17] In the acute phase of decompensated HF, however, not only the physical function but also the hemodynamics should be carefully monitored because excess physical load can increase HR and blood pressure via the overactivation of the sympathetic nervous system, leading to an increase in the afterload and risk of arrhythmia.[13] We consider this progressive mobilization program incorporating both hemodynamics and physical functional activity feasible, because it was safely implemented in all 75 patients without HF progression or any fall accidents.

In this study, physical therapy was started earlier in the intervention group than in the control group and, as a result, it ensured a sufficient intervention period until discharge, contributing to the acquirement of better ADL by discharge. Unclear protocol criteria and cumbersome protocols have been reported as barriers to the implementation of an early mobilization program in the ICU.[19] The present multidisciplinary approach to clarifying and sharing the criteria for program implementation may have removed those barriers and facilitated the program initiation. More interestingly, the present use of the progressive mobilization program enhanced the home discharge rate and resulted in a decline in the rehospitalization rate due to HF during the 1 year after discharge.

Skeletal muscle strength and mass are known to be decreased (sarcopenia) in HF,[4,20] and this condition rapidly progresses due to physical deconditioning.[21] Indeed, a study of patients hospitalized in an ICU reported that the quadriceps muscle mass, which is essential for ambulation and walking independently, sharply declines by approximately 12.5% after only 7-day bed rest.[22] The present findings therefore underscore the importance of a comprehensive and progressive mobilization program to prevent physical deconditioning in HF. The implementation of the program described herein has the potential to contribute to the improvement of discharge disposition and to a reduction in HF rehospitalization in this vulnerable population.

Compared with the patient background in previous large-scale HF registries,[23–25] the present patients were relatively older and had a higher prevalence of non-ischemic HF due to hypertension and atrial fibrillation. The overall prescription ratio of β-blockers and RAS inhibitors was relatively low, which may be due to the relatively high prevalence of HFpEF in the present study. Given that HFpEF is more common in elderly HF patients,[26] the present subjects reflect the real world of HF in the Japanese aging population. In addition, the present patients had a higher incidence of prior hospitalization for HF with multiple complications such as anemia, renal dysfunction, and stroke. One possible explanation is that this study was conducted by a single center located in a rural area in Japan, where the increase in the aged population is remarkable. In agreement with this, the mean length of hospital stay was

33 days, which was much longer than that in Western countries.[23,27] This is partly due to the difference in health-care systems, such as a lack of home-based care and rehabilitation hospitals in Japan.

In general, however, it takes a considerably long time for elderly HF patients with multiple comorbidities, who have difficulty standing without help at baseline, to achieve ambulation. Indeed, low ADL, as well as older age, anemia, and renal insufficiency, are common hospitalization risks for HF patients, and older age and hospital admission outside a city are associated with prolonged hospitalization for HF.[5,28,29] Fleming et al recently reported that early ambulation in hospitalized HF patients is related to better ADL and lower 30-day readmission rates.[7] Collectively, an aggressive mobility program targeting early ambulation is expected to improve ADL and the clinical outcome of patients with HF.

Recently, a standardized rehabilitation program for HF patients has been published by the Japanese Association of Cardiac Rehabilitation (JACR).[30] In this statement, a progressive mobilization program has also been recommended in acute phase of HF. Similar to the present intervention, the program divided the clinical course of walking ability acquisition into 6 stages, and proposed that BP, HR, SpO_2, and the presence of arrhythmia should be closely monitored at each stage increase. The proposed program, however, is not established, and is only an example, and it is stated that such a mobilization program should be modified in accordance with the patient ADL and the facility environment. Furthermore, the objective criteria for the change of stages have not been clarified. The present study provides the evidence supporting a more specific and objective mobilization program that is easily applicable for daily clinical practice.

Study Limitations

There are several limitations to be addressed. First, we were unable to analyze muscle mass and strength because these were not included in the medical records. Second, because this was a single-center and retrospective study, a selection bias may have been present, and quantitative data on physical activity and exercise capacity were not available. Finally, this study was preliminary, and did not have sufficient statistical power to determine the true efficacy or safety of the mobilization program in HF. Future prospective, large-scale, randomized studies assessing physical activity and exercise capacity would ensure the clinical efficacy of this mobilization program.

Conclusions

We have, for the first time, shown that the progressive mobilization program is safe and well tolerated in patients with acute HF. The implementation of this program was associated with not only better physical function and a shorter length of hospital stay, but also a higher rate of discharge to home and decreased readmission in HF patients. The introduction of this program is very promising in the reduction of the burden of post-admission rehabilitation care for HF.

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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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