Effects of exertional dyspnea on early mobilization of patients with acute decompensated heart failure

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Abstract. [Purpose] In this study, we investigated the association between exertional dyspnea and length of the mobilization program in patients with acute decompensated heart failure. [Participants and Methods] We recruited all consecutive patients with heart failure who were hemodynamically stabilized after administration of intravenous medication and were able to walk >10 m before admission. Exertional dyspnea was evaluated using the visual analog scale in all patients after the 10-m walk during each session of the mobilization program. Multiple regression analysis was used to determine the factors associated with length of the mobilization program. [Results] Our study included 52 patients. Multiple regression analysis showed that the length of the mobilization program was significantly associated with the visual analog scale on day 3 and the length before the start of the mobilization program; however, the length of the mobilization program showed no significant association with age and blood urea nitrogen levels. The standardized coefficients for the visual analog scale scores on day 3 and the length before the start of the mobilization program were 0.49 and 0.33, respectively. [Conclusion] Exertional dyspnea is a good predictor of the length of the mobilization program. Our findings highlight the importance of evaluation of exertional dyspnea.

Key words: Acute decompensated heart failure, Exertional dyspnea, Early mobilization

INTRODUCTION

Early mobilization is essential for rehabilitation of patients with acute decompensated heart failure (HF). The length of mobilization program leads to decreased physical function, and it is associated with significant adverse events such as quality of life¹, ², length of hospitalization³, and cardiovascular events⁴. The factors contributing to the length of mobilization program must be clarified.

Recent study have shown that age, length before the start of mobilization program, blood urea nitrogen (BUN), and ventricular tachycardia (VT) and ventricular fibrillation (VF) at admission were related to the length of mobilization program⁵⁰. However, 20–30% of patients with non-compensated HF have exacerbated HF symptoms after hospitalization⁵. Therefore, it is difficult to understand the worsening of HF symptoms and the length of mobilization program only by the index at admission. Clinicians need to evaluate post-hospitalization indicators. however, such indicators are unclear. Exertional Dyspnea, a hallmark symptom of HF, is associated with decreased cardiac output⁶, ⁷, pulmonary function due to pulmonary congestion, pleural effusion⁸, ⁹, and skeletal muscle function, such as increased muscle metabolic receptor reflexes¹⁰, ¹¹. And exertional dyspnea is related to mortality in patients with HF¹². Exertional dyspnea is associated with the pathogenesis of HF, the evaluation of exertional dyspnea may help us to predict the degree of improvement in cardiac function.
function and whether the length of mobilization program is possible. However, no study has examined exertional dyspnea in terms of the factor of the length of mobilization program in rehabilitation for patients with HF.

The purpose of this study was to identify exertional dyspnea is related to the length of mobilization program in patients with HF.

**PARTICIPANTS AND METHODS**

We conducted this study according to strengthening the reporting of observational studies in epidemiology Statement (14). We included all consecutive patients between April 2019 and April 2020 who were hemodynamically stabilized after introducing intravenous medication for HF and who were able to walk more than 10-meter (m) before admission in Shizuoka City Shimizu Hospital. We excluded patients who were unable to test and measure due to cognitive decline at admission, who died during hospitalization, or who could not obtain consent to participate in the study (Fig. 1). The medical ethics committee of Shizuoka City Shimizu Hospital approved this study (approval number: 2018-53) by the declaration of Helsinki (2013 revised version), and informed consent was obtained from all patients.

This study was a single-center prospective study. Patient characteristics, including age, gender, body mass index, etiology of HF, medication history, comorbidities, laboratory values, echocardiography, blood sampling, and chest X-rays were collected from medical records at admission (Fig. 2). On echocardiography, the left ventricular ejection fraction (LVEF) and E/e’ were measured. Hemoglobin, BUN, creatinine, glomerular filtration rate, and brain natriuretic peptide were measured by blood sampling. The cardiothoracic ratio was investigated using chest X-ray data. Urine volume and body weight from the first 10-m walk to 3 days after admission were also investigated daily from medical records. We calculated the amount of change in body weight (ΔWeight) and mean urine output difference between the weight measurements at each time point and the previous time point. Mean urine output was calculated by dividing the difference in urine output between the day of admission and the first day after the 10-m walk test was available, and between the first day (day 1) and 3 days after the first 10-m walk (day 3) by the length of days required to reach each time point.

**Fig. 1.** Schematic representation of the study cohort inclusion process.

**Fig. 2.** Measurement protocols.
We proceeded with mobilization program based on a standardized rehabilitation program for HF patients (Fig. 2). The initiation criteria for mobilization program were as follows: (1) no resting HF symptoms such as dyspnea, (2) no hemodynamically unstable arrhythmia, (3) no symptoms due to low output syndrome, (4) no state of shock, (5) no Swan-Ganz catheter insertion, and (6) no active myocardial ischemia. Mobilization program progresses in the order of the stage: sitting position, standing position, 10-m, 30-m, 50-m, 80-m, and 80-m ×3 sets every day. The criteria for not proceeding with these stages were as follows: (1) new HF symptoms, (2) increased arrhythmias, or rhythm changes to atrial fibrillation, (3) increased heartbeats (>30 beats/min), (4) a decrease in percutaneous oxygen saturation below 90%, (5) excessive blood pressure changes, and (6) ischemic ST changes. Furthermore, the Borg Scale was used as the acceptable condition for exertional dyspnea until the Borg Scale was reached. The completion of the length of mobilization program was examined as the length of days from the start program to achieve 80 m ×3 sets or the maximum continuous walking distance before admission.

We investigated exertional dyspnea using the Visual Analog Scale (VAS) after the 10-m walk. The VAS was measured for day 1 and day 3. For this assessment, patients were asked to evaluate their general well-being by marking a 10-cm vertical line, with the top labeled “no dyspnea” and the bottom labeled “worst you have ever dyspnea”. We scored the patients’ markings on a scale of 0 to 100 by measuring the distance in millimeters from the bottom of the line.

All data are shown as the mean ± standard deviation. Pearson’s product-moment correlation coefficient and Spearman’s rank correlation coefficient for the length of mobilization program and other variables were calculated. Multiple regression analysis was performed using the length of mobilization program as a dependent variable and significant variables in correlation analysis as independent variables. In the present study, in addition to the items that were significant in the correlation analysis, age, BUN, and the length before start of the mobilization program, which has been shown in previous studies to affect the length of mobilization program, were also considered independent variables. If there was a variable with a correlation coefficient of r>0.8 between the independent variables, one of them was chosen and submitted as an independent variable to avoid multicollinearity. The variable increase method with the likelihood ratio test was used to select the variables. All significant determinations were based on a risk rate of 5%. All statistical analyses were performed with SPSS Statistics Base 22.0 (Tokyo, Japan).

RESULTS

Fifty-four patients, excluding 8 who were unable to be tested and measured due to cognitive decline at admission, participated in the study. Two patients dropped out after hospitalization due to death, and there were 52 patients in the study (Fig. 1). The patient characteristics are summarized in Table 1. The mean age was 77.7 ± 11.6 years, and the body mass index was 23.6 ± 4.0 kg/m². The post-hospitalization progress in this study is summarized in Table 2. The length before start of mobilization program was 1.9 ± 1.7 days, the the length of mobilization program was 6.0 ± 4.9 days, and the length of hospital stay was 28.0 ± 12.8 days.

As shown in Table 3, the length of mobilization program was significantly correlated with the length before start of the mobilization program (r=0.41), VAS on day 1 (r=0.48), and VAS on day 3 (r=0.60). The other variables did not show a significant correlation in Table 3. VAS on day 1 and VAS on day 3 (r=0.83) showed a significant positive correlation (r>0.80). This significant positive correlation was only seen between VAS on day 1 and day 3 (p=0.05). There was no such correlation (r>0.80, and p>0.05) observed among the other independent variables. In the dependent variable of multiple logistic regression, the VAS on day 3, age, length before the start of the mobilization program, and BUN were selected to account for multicollinearity. The results of the multiple regression analysis are shown in Table 4. The length of mobilization program showed a significant relationship with VAS on day 3 and the length before the start of the mobilization program (p<0.05 for the model χ² test). The standardized coefficients for VAS on day 3 and the length before the start of the mobilization program were 0.49 and 0.33, respectively.

DISCUSSION

In this study, the length of mobilization program showed that significant relationships with the VAS score of exertional dyspnea and length before the start of mobilization program. This result suggests that exertional dyspnea may be a new index for predicting the length of mobilization program in patients with HF.

Exertional dyspnea in HF is a physical assessment that physical therapists can evaluate in routine clinical work, and it is one of the indexes that reflects the pathology of HF. Exertional dyspnea in HF is associated with two pathologies: pulmonary congestion due to increased pulmonary venous pressure and decreased blood flow to skeletal muscles. In patients with HF, exertional dyspnea reflects various pathologies of cardiac, pulmonary, and skeletal muscle function, and the degree of exertional dyspnea in the early phase of hospitalization might reflect the extent of these pathologies. As HF gets worse and fluid collects, most people will have stronger exertional dyspnea. When the HF status is worse, the length of the mobilization program were longer. Therefore, the stronger exertional dyspnea is, the longer the length of mobilization program.
In clinical work, a patient who will be longer the length of mobilization program needs additional individualized interventions to prevent deconditioning\(^{22}\). Recent studies have shown that endurance training\(^{23–25}\), resistance training\(^{24, 25}\), physical activity\(^{26–28}\), neuromuscular electrical stimulation\(^{29–31}\), and leg cycles\(^{32}\) are effective in treating patients with HF. Such interventions for patients with HF may prevent poor physical function, poor quality of life\(^{1, 2}\), and longer hospital stays\(^{3}\). In cases that delay mobilization program, individualized additional interventions might be necessary.

In conclusion, exertional dyspnea in the early phase of hospitalization was significantly associated with the length of mobilization program. This study has several limitations. First, some participants in this study were characteristic. Participants in this study were more likely to have heart failure patients with congestive pathology than with cardiogenic shock\(^{33, 34}\).

| Table 1. Patient characteristics |
|----------------------------------|
| Research items                    | All participants |
| n                                | 52               |
| Age, years                       | 77.7 ± 11.6      |
| Male, n (%)                      | 31 (60)          |
| BMI, kg/m\(^2\)                  | 23.6 ± 4.0       |
| NYHA class (II/III/IV), n (%)    | 4 (8)/25 (48)/23 (44) |
| Etiology of HF                   |                  |
| Ischemic heart disease, n (%)    | 11 (22)          |
| Valvular heart disease, n (%)    | 11 (22)          |
| Hypertension, n (%)              | 11 (22)          |
| Dilated cardiomyopathy, n (%)    | 4 (8)            |
| Other, n (%)                     | 14 (26)          |
| Medical history                  |                  |
| Hypertension, n (%)              | 36 (69)          |
| Diabetes, n (%)                  | 13 (25)          |
| Chronic kidney disease, n (%)    | 9 (18)           |
| Chronic obstructive pulmonary disease, n (%) | 8 (16) |
| Atrial fibrillation, n (%)       | 19 (36)          |
| History of hospitalization for HF, n (%) | 13 (25) |
| Cardiothoracic ratio (%)         | 57.8 ± 7.4       |
| LVEF (%)                         | 51.8 ± 14.1      |
| E/e'                             | 17.4 ± 5.0       |
| Hemoglobin, mg/dL                | 11.8 ± 2.6       |
| BUN, mg/dL                       | 26.3 ± 11.8      |
| Cr, mg/dL                        | 1.31 ± 0.50      |
| eGFR, mL/min/1.73 m\(^2\)        | 43.4 ± 14.2      |
| BNP, pg/dL                       | 696.9 ± 460.2    |
| Dopamine hydrochloride, n (%)    | 1 (2)            |
| Dobutamine hydrochloride, n (%)  | 7 (13)           |
| Noradrenaline, n (%)             | 0 (0)            |
| PDE–inhibitor, n (%)             | 0 (0)            |
| Nitrate, n (%)                   | 12 (23)          |
| Carperitide, n (%)               | 35 (68)          |
| Loop diuretic, n (%)             | 50 (97)          |
| NPPV, n (%)                      | 7 (13)           |
| Cardiopulmonary support, n (%)   | 0 (0)            |
| Acute blood purification therapy, n (%) | 0 (0) |

Data are presented as mean ± SD or n (%). BNP: brain natriuretic peptide; BMI: body mass index; BUN: blood urea nitrogen; Cr: creatinine; E/e': early diastolic mitral annulus velocity (e') estimated by tissue Doppler and the ratio of the trans-mitral early peak velocity (E) by pulsed wave Doppler over e'; eGFR: estimated glomerular filtration rate; LVEF: left ventricular ejection fraction; NPPV: noninvasive positive pressure ventilation; NYHA: New York Heart Association; PDE, phosphodiesterase.
### Table 2. Post-hospitalization progress

| Research items                                      | All participants |
|-----------------------------------------------------|------------------|
| ΔWeight, kg                                          |                  |
| From hospitalization to day 1                        | −1.3 ± 2.5       |
| From day 1 to day 3                                  | −1.0 ± 1.2       |
| Average urine output, ml                             |                  |
| From hospitalization to day 1                        | 2,742.1 ± 2,173.2|
| From day 1 to day 3                                  | 1,606.3 ± 1,107.6|
| Dyspnea on exertion VAS, mm                          |                  |
| VAS on day 1                                         | 22.4 ± 18.1      |
| VAS on day 3                                         | 15.3 ± 18.0      |
| The length before start of mobilization program, day | 1.9 ± 1.7        |
| The length of mobilization program, day              | 6.0 ± 4.9        |
| The length of hospital stay, day                     | 28.0 ± 12.8      |

Data are presented as mean ± SD or n (%). Δweight: weight change; VAS: visual analog scale.

### Table 3. Correlation with the length of mobilization program

| Research items                                      | r                |
|-----------------------------------------------------|------------------|
| Age                                                 | 0.90             |
| BMI                                                 | −0.08            |
| NYHA class                                           | 0.26             |
| Cardiothoracic ratio                                | 0.37             |
| LVEF                                                | 0.15             |
| E/e’                                                | −0.08            |
| Hemoglobin                                          | −0.18            |
| BUN                                                 | 0.14             |
| Cr                                                  | 0.03             |
| eGFR                                                | −0.30            |
| BNP                                                 | 0.11             |
| Hospitalization for HF in past                      | −0.30            |
| The length before start of the ambulation           | 0.41*            |
| VAS on Day 1                                         | 0.48*            |
| VAS on Day 3                                         | 0.60*            |
| ΔWeight from hospitalization to day 1                | −0.17            |
| ΔWeight from day 1 to day 3                          | −0.57            |
| Average urine output from hospitalization to day 1   | −0.80            |
| Average urine output from day 1 to day 3             | −0.13            |

*p<0.05.

BMI: body mass index; BNP: brain natriuretic peptide; BUN: blood urea nitrogen; Cr: creatinine; E/e’: early diastolic mitral annulus velocity (e’) estimated by tissue Doppler and the ratio of the trans−mitral early peak velocity (E) by pulsed wave Doppler over e’; eGFR: estimated glomerular filtration rate; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; r: correlation coefficient; VAS: visual analog scale; ΔWeight: weight change.

### Table 4. Multiple regression analyses on the length of mobilization program

| Research items                                      | b     | 95% CI            |
|-----------------------------------------------------|-------|-------------------|
| VAS on Day 3                                         | 0.49  | 0.06−1.21*        |
| Age                                                 | 0.21  | 0.02−0.58         |
| The length before the start of mobilization program  | 0.33  | 0.19−1.62*        |
| BUN                                                 | 0.45  | 0.36−0.76         |

*p<0.05.
b: standardized regression coefficient; BUN: blood urea nitrogen; CI: confidence interval; VAS: visual analog scale.
Additional studies on patients with HF, mainly due to low cardiac output, are needed. Second, the survey was conducted by a single institution, which may lead to selection bias. Third, factors influencing exertional dyspnea need to be studied further. Unmeasured confounding factors might have affected the results in the length of mobilization program. Fourth, this study may not be sufficiently blinded. Dyspnea is a subjective assessment, which may lead to measurement bias. Therefore, blinding is desirable. This study suggests that exertional dyspnea is a good predictor of mobilization program. HF patients with severe exertional dyspnea in the early phase of hospitalization should be considered for individualized interventions in addition to early mobilization.

Conflict of interest
All authors declare no conflicts of interest.

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