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Effects of early mobilisation program on functional capacity, daily living activities, and N-terminal prohormone brain natriuretic peptide in patients hospitalised for acute heart failure. A randomised controlled trial

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Background: Patients hospitalised for acute decompensated heart failure (ADHF) show reduced functional capacity, limited activities of daily living (ADL), and elevated N-terminal prohormone of brain natriuretic peptide (NT-proBNP). The management of these patients focuses mainly on medical therapy with little consideration for in-patient cardiac rehabilitation. There has been a growing interest in evaluating the efficacy of early mobilisation, as the core for in-hospital rehabilitation, in ADHF patients in the last decade; however, the randomised trials on this topic are few.
Objective: This randomised-controlled study, therefore, aimed to further test the hypothesis that early supervised mobilisation would have beneficial effects on functional capacity, ADL, and NT-proBNP in stabilised patients following ADHF.

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Methods: This is a single-centered, randomised-controlled, parallel-group trial in which 30 patients hospitalised for ADHF were randomly assigned to two groups; the study group (age = 55.4 ± 5.46 years, $n_1 = 15$) and the control group (age = 55.73 ± 5.61 years, n_2=15). Inclusion criteria were ADHF on top of chronic heart failure independent of etiology or ejection fraction, clinical/hemodynamic stability, age from 40 to 60 years old, and both genders. Exclusion criteria were cardiogenic shock, acute coronary ischemia, or significant arrhythmia. Both groups received the usual medical care, but only the study group received an early structured mobilisation protocol within 3 days of hospital admission till discharge. The outcome measures were the 6-min walk distance (6-MWD) and the rating of perceived exertion (RPE) determined from the 6-min walk test at discharge, the Barthel index (BI), NT-proBNP, and the length of hospital stays (LOS).
Results: The study group showed significantly greater improvements compared to the controls in the 6-MWD (252.28 ± 92.32 versus 106.35 ± 56.36 m, $P < 0.001$), the RPE (12.53 ± 0.91 versus 15.4 ± 1.63, $P < 0.001$), and the LOS (10.42 ± 4.23 versus 16.85 ± 6.87 days, $p = 0.009$) at discharge. Also, the study group showed significant improvements in the BI compared to baseline [100 (100–100) versus 41.87 (35–55), $p = 0.009$] and the controls [100 (100–100) versus 92.5(85–95), $p = 0.006$]. The mean value of NT-proBNP showed a significant reduction only compared to baseline (786.28 ± 269.5 versus 1069.03 ± 528.87 pg/mL, $p = 0.04$) following the intervention. The absolute mean change (Δ) of NT-proBNP showed an observed difference between groups in favor of the study group (i.e., $\Delta = \downarrow 282.75 \pm 494.13$ pg/mL in the study group versus $\downarrow 26.42 \pm 222.21$ pg/mL in the control group, $p = 0.077$).
Conclusion: Early structured mobilisation under the supervision of a physiotherapist could be strongly suggested in combination with the usual medical care to help improve the functional capacity and daily living activities, reduce NT-proBNP levels, and shorten the hospital stay in stabilised patients following ADHF. Trial registration number: PACTR202202476383975.

Keywords: Acute heart failure; cardiac rehabilitation; early mobilisation; 6-min walk test; daily living activities; NT-proBNP.

Introduction

Heart failure (HF) is considered a major clinical problem and public health concern.[1] Recent epidemiological studies suggest that the occurrence of heart failure did not increase globally, but the mortality and hospitalisation associated with the disease have continued to increase despite enormous management efforts.[1] Acute decompensated heart failure (ADHF) can be defined as acute decompensation of cardiac function and/or worsening of heart failure signs and symptoms with an urgent need for hospitalisation.[2] Hospitalised patients with ADHF most commonly suffer from severe breathlessness, fatigue, lower limb muscle weakness, and increased weight from peripheral edema, resulting in reduced functional capacity, poor tolerance to physical activity, and impairment in activities of daily living (ADL).[2,3] The physical dysfunction in these patients worsens further from prolonged hospital stay and bed rest,[4] and can persist even after the restoration of the symptoms and signs of acute HF. The physical disabilities in ADHF patients are probably not fully managed by routine medical/pharmacological treatment which mainly targets the adequacy of hemodynamic stability and organ perfusion. Not to mention that the referral to cardiac rehabilitation programs is poor in clinical practice and has further reduced after the COVID-19 pandemic.[5,6] Therefore, the need for in-hospital cardiac rehabilitation in addition to standardised medical care should be emphasised.

Early mobilisation is the main component of early cardiac rehabilitation and is closely related to favourable clinical outcomes.[7] Early mobilisation refers to the gradual changing of patients' positions from a supine or slumped position in bed to an upright sitting in a bedside chair, which is then progressed to standing, walking and stair climbing.[8,9] This should be started as soon as the clinical stability of the patient is ensured.[8,9] In the past, most of the rehabilitation-based research work included chronic heart failure patients and excluded hospitalised patients with recently acute HF.[10,11] In the last decade, there has been an increased interest in the evaluation of the safety and efficacy of early mobilisation programs in ADHF patients by a considerable number of studies.[7,9,12–25]

Collectively, these studies demonstrated that early structured mobilisation in stabilised patients hospitalised for acute HF was safe and effective in increasing functional capacity, improving ADL, shortening the hospital stay time, and reducing the re-hospitalisation rate. Nevertheless, apart from the recent randomised study by Kitzman *et al.*[24] there have been only four randomised controlled trials on the topic of early mobilisation in patients with acute HF,[12,14,16,21] based on a recent systematic review by Babu *et al.*[26] They concluded that the research work in this field is still growing, and further intervention studies are to be suggested.[26]

Several outcome measures can be of importance when assessing the clinical benefits of early mobilisation in hospitalised acute HF patients. The most important measure is the patients' functional capacity which could be a better prognostic indicator of disease progression or re-hospitalisation than cardiac function.[27] A reduced functional capacity prohibits patients from being physically active which leads to a further reduction in their functional capacity in "a vicious circle" manner. The six-minute walk test (6-MWT) is the most frequently used test to assess patients' functional capacity in heart failure patients.[28] The distance covered during the 6-MWT is the primary outcome of the test, but also dyspnea response to the test measured by the rating of perceived exertion (RPE) scale represents another important measure. To add, the Barthel index (BI) is a standardised tool used to assess the capabilities of ADL in hospitalised acute HF patients and to predict the treatment outcomes.[18,29,30] Furthermore, the N-terminal pro-B-type natriuretic peptide (NT-proBNP) is one of the gold standard biomarkers for the presence and severity of cardiac hemodynamic overload and failure.[31] NT-proBNP can help evaluate the response to therapy and predict the clinical outcome in patients with HF.[32]

Considering the few numbers of randomised controlled trials evaluating the efficacy of early mobilisation in hospitalised patients for acute HF, as previously mentioned, this randomised-controlled study aimed to further evaluate the effects of early physiotherapist-supervised mobilisation program on functional capacity assessed by 6-MWT, ADL assessed by BI, and cardiac hemodynamic function, assessed by NT-proBNP (as primary outcomes); as well as the hospital stay time (as a secondary outcome) in stabilised HF patients following acute decompensation of heart function. We hypothesised that early mobilisation could be effective in improving these clinical outcomes in this patient population based on the findings from the previous studies. The results of this study could help highlight the clinical significance of early mobilisation in stabilised patients following ADHF and aid strengthen the evidence base for the in-patient phase of cardiac rehabilitation in this population.

Methods

This study was reported as per the CONSORT 2010 Statement for reporting randomised trials.

Study design and settings

This is a single-centered, randomised controlled, parallel-group intervention study. This study was conducted at the Cardiology Department of Kasr Alainy Hospital from March 2021 to September 2021. The study obtained ethical approval from the Ethics Committee of Scientific Research of the main author's institution (approval No. 012/003090) and followed the principles laid down by the declaration of Helsinki. Informed consent was obtained from patients before the intervention.

Randomisation and concealed allocation

Simple randomisation using a randomisation table designed by a computer software program was used in this study with an allocation ratio of 1:1. Sequentially numbered opaque sealed envelopes (SNOSE) were used to conceal the allocation sequence so that neither the researcher nor the participant was aware of the upcoming assignment.

Sample size calculation

The sample size was calculated from the previously published data,[16] for the primary outcome measure (i.e., 6-MWD). At a p-value of less than 0.05 and a power of 80%, the sample size (n) was calculated as $n = 2\ \mathrm{SD}^2\ (Z_{\alpha/2} + Z_{\beta})^2/d^2$, according to Charan and Biswas,[33] where $Z_{\alpha/2} = 1.96$ for two tailed results at $p < 0.05$; $Z_{\beta} = 0.84$ for a power of 80%; SD = Standard Deviation (pooled SD of the 6-MWD) = 29.15 m;[16] d = expected effect size = mean change of the 6-MWD in the intervention

group (Δ 73 m) – mean change of the 6-MWD in the control group (Δ 45 m) = 28 m.[16] Accordingly, $n = 2\ (29.15)^2 \times (1.96 + 0.84)^2 \div (28)^2 = 17$. Accordingly, the minimum sample size was estimated to be 17 patients per group. But, to account for a 10–20% drop-out rate, we recruited a total of 20 patients per group.

Subjects

Thirty hospitalised acute HF patients, out of 40 patients, underwent the final analysis of the study. They were recruited in this study by referral from a cardiologist. Eligibility criteria were patients hospitalised for acute decompensation of chronic heart failure independent of etiology or ejection fraction, age from 40–60 years old, both gender, and hemodynamic/clinical stability. Exclusion criteria were unstable vital signs, cardiac arrhythmia, critical illness, ongoing cardiogenic shock or inotropic therapy, post-surgical patients, acute myocardial ischemia, locomotor/neurological limitations to ambulation, cognitive impairment, and patients on high FiO_2, or continuous oxygen therapy. Eligible patients were randomly assigned either to a study or a control group. Both groups were under the usual medical care, but only the study group received a supervised mobilisation program. The flow of subjects throughout the study can be shown in Fig. 1.

Evaluations

Clinical examination and history taking

These were done by a specialised cardiologist. The age, weight, and other clinical characteristics of patients were reported.

Six-minute walk test

The 6-MWT was conducted for all patients under the standardised procedure reported by the European Respiratory Society and the American Thoracic Society,[34] at discharge.[21] The 6-MWT was performed indoors along a flat, straight, enclosed corridor with a hard surface. The walking track was 30 m in length, marked every 10 m. The equipment used was mainly a countdown timer,

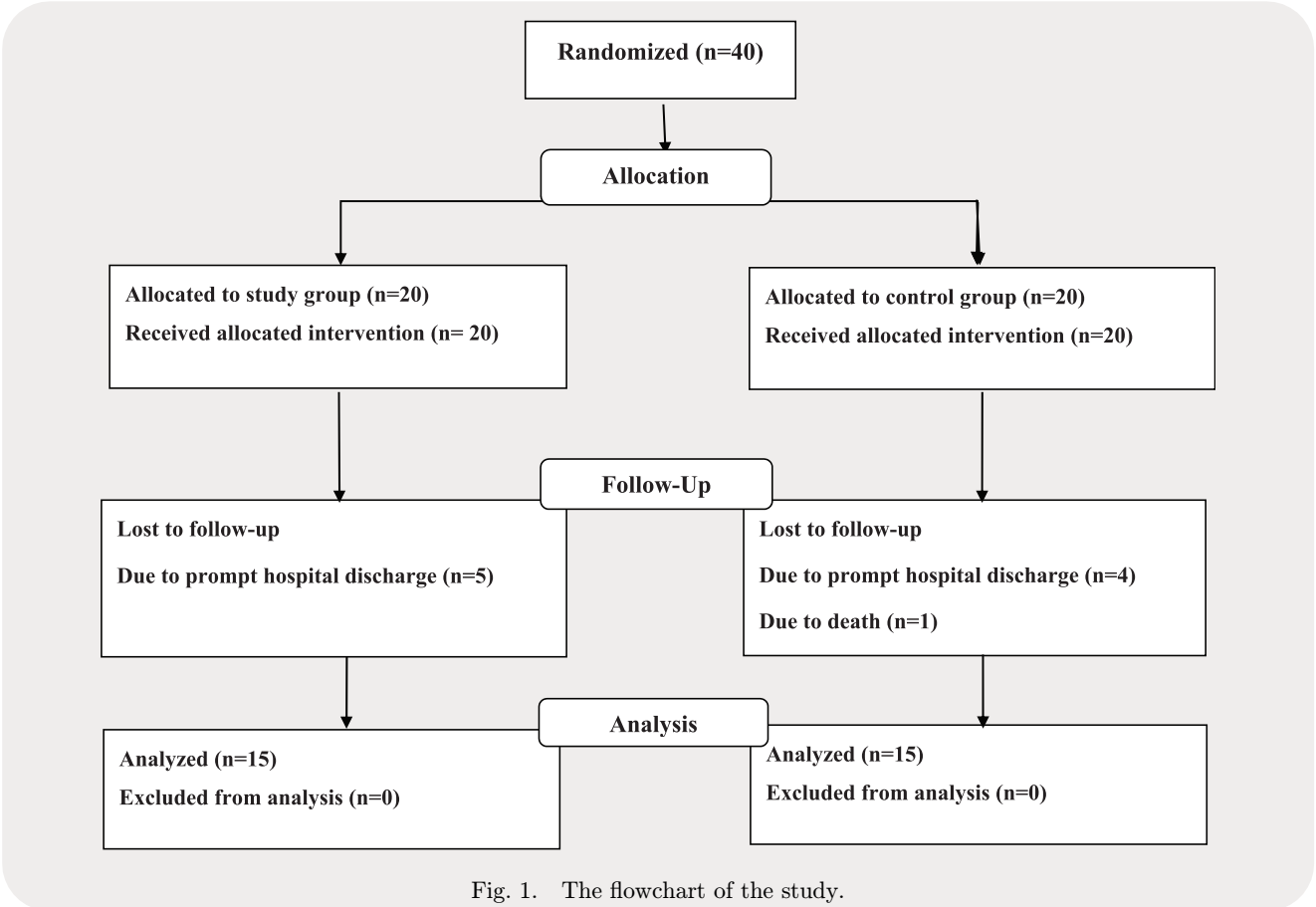

Fig. 1. The flowchart of the study.

the RPE scale, and a fingertip pulse oximetry to record heart rate and oxygen saturation (SpO_2) before, during, and after the test. Patient preparation included comfortable clothing and proper footwear, avoidance of exhausting physical activity within 2 h before the test, and adherence to the usual medications. Before the test, the instructions given to patients were to walk (not to jog or run) as far as possible for 6 min, to walk back and forth, to slow down or stop and rest when becoming exhausted or out of breath, to lean against the wall or sit down while resting, and to resume walking as soon as possible. During the test, standardised phrases of encouragement were utilised every minute as per the guidelines,[34] and the heart rate and oxygen saturation were continuously monitored by a fingertip pulse oximeter (Granzia, Pulsox-304, Italy). The test was terminated upon the patient request to stop or when 6 min passed. At this point, the RPE was recorded and the distance covered during the test [i.e., the 6-min walk distance (6-MWD)] was measured.

Barthel index

The BI was used as a standardised tool to assess the ADL[30] in the two groups at baseline and discharge. BI comprises 10 items divided into two categories: those assessing self-care (i.e., feeding, bathing, grooming, dressing, bowel & bladder care, and toilet use,) and others assessing mobility (i.e., transfers, ambulation, and stair climbing),[30] as shown in Appendix A. Each item was scored as described in Appendix A and the total sub-scores of the 10 items were summated to get a total score out of 100. A score of zero represents completed dependency and a score of 100 represents complete independence.

N-terminal pro-brain natriuretic peptide (NT-proBNP)

At baseline and before the discharge, venous blood samples were taken from patients and the NT-proBNP concentrations were assessed using the enzyme-linked immunosorbent assay (ELISA) technique according to the manufacturer's instructions (SinoGeneClon Biotech Co., Ltd, Human NT-proBNP Elisa Kit, China, No: SG-10015).

Length of hospital stays (LOS)

This was the hospitalisation period in days from the day of admission to the day of discharge. The LOS was used in this study as a quality metric.

Interventions

Usual medical care

All patients in the two groups received standard medical treatment as per the guidelines.[35] Medications were prescribed by a cardiologist and included diuretics, ACE Inhibitors/ARBs, Beta-Blockers, calcium channel blockers, digoxin, anti-platelets agents, anti-hyperglycemic agents, and statins. The medications in the two groups are listed in Table 2. Selected patients in both groups received chest physiotherapy (i.e., respiratory exercises and huffing/coughing) upon need.

Mobilisation program

Patients in the study group received in-patient cardiac rehabilitation as an early structured mobilisation program supervised closely by a physiotherapist in combination with the usual medical care within the first three days of hospital admission. The mobilisation program started as soon as the clinical stability of patients allowed and continued gradually throughout the hospitalisation period until discharge. The mobilization protocol was designed individually according to the (*Frequency, Intensity, Time, Type* (FITT) principle) reported by the recent guidelines of the European Society of Cardiology[36] (Table 1). The intensity of mobilisation activities was low to moderate at a target heart rate that equaled the resting heart rate plus 20–30 beats/min,[37] monitored objectively by a finger pulse oximeter (Granzia, Pulsox-304, Italy). Also, the targeted intensity was guided by the patient's perceived exertion and set at a RPE of 11–13 on a 20-point Borg scale.[36,37] The mobilisation program, including the frequency & duration of the sessions and the type of physical activities at each stage, can be shown in detail in Table 1. The criteria for terminating the mobilisation sessions were any symptoms or signs suggesting postural hypotension, intolerance to physical activity, or poor central/peripheral perfusion such as dizziness, blurred vision, confusion, severe breathlessness or fatigue, chest pain, palpitations, leg cramp, cold sweating, pallor, $>4\%$ decrease in O_2 saturation, cyanosis, or exaggerated heart rate response.[8,17] The mobilisation session progressed to the next stage once the patient was clinically stable during and after the premier stage (i.e., absence of the above-mentioned signs and symptoms plus: absence of new-onset arrhythmia,

Table 1. The prescription of the structured mobilisation program.

FITT[a] Concept	Stages				
	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5
Frequency Sessions/week Sessions/day	Daily Twice/day	Daily Twice/day	Daily Twice/day	Daily Twice/day	Daily Twice/day
Intensity, monitored by: THR[b] RPE[c] on a 20-point scale	THR = Resting HR[d] + 20 (beats/min) RPE = 11–12	THR = Resting HR + 20 (beats/min) RPE = 11–12	THR= Resting HR + 20 (beats/min) RPE = 11–12	THR = Resting HR + 20-30 (beats/min) RPE $\leq$ 13	THR = Resting HR + 30 (beats/min) RPE $\leq$ 13
Time/Duration	< 10 min	< 10 min	3–5 min	5–10 min	5–15 min
Type/mode	1-Active free dynamic exercises for the upper and lower limbs from supine & sitting [1–3 sets, 5–10 reps/set]. -For the upper limbs: elbow flexion & extension, shoulder flexion & extension, shoulder abduction & adduction, Scapular retraction. -For the lower limb: dorsiflexion & plantar flexion, knee flexion & extension, hip flexion & extension, hip abduction & adduction. 2-Strength exercise: sit-to-stand exercises (1 set, 10 reps/set)	1-Active free dynamic exercises for the upper and lower limbs (i.e., the same as in stage 1 but from standing) 2-Balance exercises From sitting & standing. (e.g. patient tried to maintain balance while in sitting or standing positions against a gentle push in all directions from the therapist.	Endurance exercise: Walking	Endurance exercise: Walking	1-Endurance exercise: Walking 2- Endurance & strength exercise: stair climbing (one floor)

Notes: [a]Frequency, Intensity, Time, and Type.
[b]Target Heart rate.
[c]Rating of perceived exertion.
[d]heart rate

no worsening of edema, no worsening of dyspnea or fatigue, and no reduction of urine output), as reported by Kakutani *et al.*[17] It is worth noting that the mobilisation program was designed based on stages and not days, as shown in Table 1.

Statistical analysis

Data underwent descriptive statistics and presented as means ± standard deviations, frequencies & percent distributions, and medians & interquartile range. For continuous variables, the Kolmogorov–Smirnov test assessed the normality of distribution, and the Levene's test evaluated the homogeneity of variance between groups. Data with normal distribution underwent parametric statistics, and the Paired *t*-test analysed the changes within each group post-intervention. For normally distributed data with equal variance between groups, the unpaired *t*-test analysed the difference in the mean values of variables between the two groups. For normally distributed data with unequal variance between groups (i.e., LOS), Welch's *t*-test analysed the difference in the means between the two groups. Data with an abnormal distribution that failed the normality test after data transformation (i.e., BI data) underwent non-parametric statistics. Wilcoxon signed-rank test analysed the changes within each group, and the Mann–Whitney U test analysed the difference between the two groups pre- and post-intervention. For categorical variables (i.e., gender and clinical characteristics), the Fisher exact test assessed the difference between the two groups at baseline. Absolute mean change (Δ) from baseline, in the NT-proBNP, was analysed as an independent variable and compared between the two groups using the Unpaired *t*-test. A significance level of $p < 0.05$ was utilised in all statistical tests. The statistical analysis was conducted by the Statistical Package of Social Science (SPSS) statistics software program version 25 for Windows (SPSS, Inc., Chicago, IL).

Results

At baseline, there were non-significant differences between the two groups in the patients' demographic, anthropometric, or clinical characteristics and medications, as shown in Table 2. Compared to the control group, the study group showed significantly greater improvements in the 6-MWD (252.28 ± 92.32 m in the study group versus 106.35 ± 56.36 m in the control group, $p < 0.001$, Unpaired *t*-test), the RPE (12.53 ± 0.91 in the study group versus 15.4 ± 1.63 in the control group, $p < 0.001$, Unpaired *t*-test), and the LOS (10.42 ± 4.23 days in the study group versus 16.85 ± 6.87 days in the control group, $p = 0.009$, Welch's *t*-test) following the intervention. The study group also showed significant improvements in the BI scores compared to baseline [100 (100–100) versus 41.87 (35–55), $p = 0.009$, Wilcoxon signed-rank test] and the controls [100 (100–100) versus 92.5 (85–95), $p = 0.006$, Mann–Whitney U test]. In addition, the study group showed a significant reduction in the mean value of NT-proBNP compared to baseline only (786.28 ± 269.5 pg/mL versus 1069.03 ± 528.87 pg/mL, $p = 0.04$, Paired *t*-test). Further, this study showed an observed difference in the absolute mean change (Δ) of NT-proBNP between the two groups in favor of the study group with a tendency towards significance (i.e., $\Delta = \downarrow 282.75 \pm 494.13$ pg/mL in the study group versus $\downarrow 26.42 \pm 222.21$ pg/mL in the control group, $p = 0.077$, Unpaired *t*-test).

Discussion

In agreement with our hypothesis, this study showed that early supervised mobilisation in combination with the usual medical care resulted in more improvements in the 6-MWD and RPE derived from the 6-MWT, more enhancement in ADL assessed by BI, and shorter hospital stay compared to usual medical care alone, in stabilised patients who were hospitalised for acute decompensated HF. This study also showed that early mobilisation combined with medical care led to statistically and clinically significant reductions in the NT-proBNP compared to pre-intervention levels in these patients.

Concerning the functional capacity, this study showed that the early mobilisation combined with the usual medical care led to significantly more improvements in the 6-MWD and the RPE post 6-MWT compared to the medical care alone. In agreement with these findings, Babu *et al.*[12] found that the 6-MWD increased significantly at discharge in hospitalised HF patients who underwent phase I cardiac rehabilitation compared to patients in the control group. Also, Delgado *et al.*[21]

Table 2. Baseline characteristics.

Characteristics		Study group ($n_1 = 15$)	Control group ($n_2 = 15$)	p-Value
Age (years)		55.4 ± 5.46	55.73 ± 5.61	0.871
Gender	Males	12 (80%)	8 (53%)	0.245
	Females	3 (20%)	7 (47%)	
Body mass index (kg/m^2)		27.64 ± 4.05	26.79 ± 7.21	0.693
Ejection fraction (%)		34.2 ± 12.43	37.2 ± 14.05	0.540
NYHA Classification	Class III	9 (60%)	8 (53%)	> 0.99
	Class IV	6 (40%)	7 (47%)	
Heart failure	Left-sided	13 (86.6%)	13(86.6%)	> 0.99
	Right-sided	2 (13.3%)	2(13.3%)	
Diabetes		8 (53.3%)	10 (66.7%)	0.710
Hypertension		7 (46.7%)	10 (66.7%)	0.462
Smoking history		7 (46.7%)	4 (26.7%)	0.449
Chest infection		6 (40%)	8 (53.3%)	0.715
Atrial fibrillation		4 (26.7 %)	3 (20%)	> 0.99
Dilated cardiomyopathy		4 (26.7%)	5 (33.3%)	> 0.99
Ischemic cardiomyopathy		9 (60%)	8 (53.3%)	> 0.99
Medications				
Diuretics		11 (73.3%)	11 (73.3%)	> 0.99
ACE Inhibitors/ARBs		2 (13.3%)	6 (40%)	0.214
Beta-blockers/calcium channel blockers		7 (46.7%)	7 (46.7%)	> 0.99
Digoxin		3 (20%)	4 (26.7%)	> 0.99
Anti-platelets/Anti-coagulants		13 (86.7%)	11 (73.3%)	0.651
Anti-hyperglycemic		8 (53.3%)	10 (66.7%)	0.710
Statins		8 (53.3%)	6 (40%)	0.715

Notes: Data are expressed as means ± standard deviations and as frequencies and percent distributions. The Unpaired t-test was used to analyze continuous variables between groups. The Fisher exact test was used to analyze the unpaired proportions between the two groups.

reported that the 6-MWD showed significantly more improvement at discharge following an early mobilisation protocol in hospitalised patients for acute HF. They also found that the breathlessness that limits daily activities in these patients, assessed by the London chest activity of daily living (LCADL) scale, has reduced significantly in the intervention group compared to the control group.[21] In addition, Oliveira *et al.*[16] showed that low-intensity exercise using unloaded in-bed cycle ergometer resulted in more significant improvements in 6-MWD compared to the controls and more reduction in dyspnea compared to baseline in acute HF patients. Further, Takada *et al.*[22] found that early rehabilitation (within three days of admission) led to higher capability for unassisted walking in hospitalised patients with acute HF compared to those who received rehabilitation lately. Notably, an increase of > 50 m in the 6-MWD following in-patient rehabilitation has been considered a clinically meaningful outcome for hospitalised HF patients and significantly related to a reduced risk for a 3-year mortality post-discharge.[38] On the contrary, according to a recent meta-analysis by Fuentes-Abolafio *et al.*[39] HF patients with poor 6-MWT performance are at a higher risk for all-cause mortality on the whole and cardiovascular mortality in specific. It is worth noting that dyspnea was associated with unfavorable clinical outcomes in patients with acute HF.[20] So, we can suggest that the reduction in the RPE following early mobilisation in our study could be associated with other favorable outcomes such as better BI and shorter LOS.

Another finding in this study was the significant improvement in the ADL, evidenced by higher BI scores, following the early mobilisation program compared to baseline and the controls. Per this, Motoki *et al.*[18] found that the median BI scores increased significantly compared to baseline after

Table 3. Results of the two groups pre- and post-interventions.

Outcome measures			Study group ($n_1 = 15$)	Control group ($n_2 = 15$)	p-value
6-MWT[a]	6-MWD[b] (meters)	At discharge	252.29 ± 95.81	106.36 ± 58.49	< 0.001**
	RPE[c] (a 20-point Borg scale)	At discharge	12.53 ± 0.91	15.4 ± 1.63	<0.001**
Barthel index (0–100)		Baseline	41.87 (35–55)	30 (20–40)	0.155
		At discharge	100 (100-100)	92.5 (85-95)	0.006‡
		p-value	0.009‡	0.031‡	
NT-proBNP[d] (pg/ml)		Baseline	1069.03 ± 528.87	973.63 ± 261.45	0.536
		At discharge	786.28 ± 269.5	947.21 ± 341.91	0.163
		Δ	−282.75 ± 494.13	−26.42 ± 222.21	0.077
		p-value	0.043*	0.652	
LOS[e] (days)		At discharge	10.43 ± 4.40	16.86 ± 7.13	0.009§

Notes: Data are expressed as means ± standard deviations and as medians and inter-quartile range. [a]6-min walk test; [b]6-min walk distance; [c]rating of perceived exertion. [d]N-terminal prohormone of brain natriuretic peptide; [e]length of hospital stays. **significant p-value based on the Unpaired t-test. *significant p-value based on Paired t-test. ‡significant p-value based on the Wilcoxon signed-rank test. ‡significant p-value based on the Mann–Whitney U test. §significant p-value based on Welch's t-test. Δ: absolute mean change.

an in-patient cardiac rehabilitation program in patients following acute HF. Also, Kakutani *et al.*[17] showed that a progressive mobilisation program resulted in a significantly higher BI score than the control group in hospitalised acute HF patients. In addition, Delgado *et al.*[21] recorded a more observed increase in the BI score in hospitalised HF patients who received early mobilisation than in the controls. Furthermore, in a large retrospective study by Suzuki *et al.*[19] early rehabilitation showed a negative association with BI deterioration and positively related to maintenance of ADL. To be mentioned, since the decline in the ADL by acute HF has been an independent risk factor for major cardiovascular events,[3] it is reasonable to assume that the improved ADL following the mobilisation program in this study may have a long-term protective effect against these events.

This study also showed that the mean value of NT-proBNP has reduced significantly in the study group compared to baseline only. In agreement with this finding, Oliveira *et al.*[16] showed that bedside low-intensity exercises induced a significant reduction in the NT-proBNP compared to baseline and not to the controls. In addition, this study revealed that the Δ NT-proBNP was more in the study group than in the control group and was somewhat close to the significance level ($p = 0.077$). Interestingly, although the NT-proBNP did not return to its normal levels following the mobilisation program in this study, its mean value showed a significant reduction from 1069.03 ± 528.87 pg/mL to 786.28 ± 269.5 pg/mL. This reduction can be of clinical significance in our patients aged 55.4 ± 5.46 years. As per Januzzi *et al.*[40] the NT-proBNP levels below 900 pg/mL for patients ≥ 50 indicate stabilised cardiac functioning in acute HF patients. Not to forget that the positive changes in the NT-proBNP concentrations are more clinically meaningful when supported by other positive changes in a functional outcome such as 6-MWD.[41]

Unsurprisingly, this study revealed that early mobilisation led to shorter hospital stays in patients hospitalised for acute HF. Fleming *et al.*[15] found that the earlier the ambulation is, the less the hospitalisation period and the lower the incidence of hospital readmission. Also, Oliveira *et al.*[16] found that patients in the intervention group had an earlier hospital discharge compared to the controls. In addition, Kakutani *et al.*[17] showed that acute HF patients who received early progressive mobilisation had a significantly shorter hospital stay than other patients who did not. Likewise, Kaneko *et al.*[23] reported that acute-phase (within two days of admission) rehabilitation related to a shorter hospital stay in patients with acute HF.

To be mentioned, in the study group, one patient experienced dehydration, and another patient had a drug-induced long QT syndrome. Both patients were admitted to the cardiac care unit, and then, they resumed the mobilisation activities after being clinically stable as per the cardiologist's decision. Otherwise, no major cardiovascular events, adverse effects, or falls were reported during or after the early mobilisation program. Previous studies also reported no significant cardiac events following mobilisation programs in stabilised acute HF patients,[15–18,21] indicating that mobilisation can safely start for these patients at the earliest provided that strict patient selection and close monitoring are ensured.

The clinical implications of this study are several. This study extends knowledge about the efficacy of early physiotherapist-supervised mobilisation to clinicians dealing with acute HF patients. The limited knowledge or the uncertainty about its benefits or safety can be potential reasons for the poor referral to in-patient cardiac rehabilitation (CR).[42] Also, since limited resource is another major cause for not referring patients to CR in low- and middle-income countries,[6] supervised mobilisation appears to be a cost-effective intervention in such circumstances requiring minimal equipment. Furthermore, as a simple intervention, early mobilisation under the supervision of experienced physiotherapists can have good applicability to real-world practice. Moreover, not only the early mobilisation is beneficial in terms of improved functional ability and independence of HF patients at discharge, but also it provides a good opportunity for engaging in out-patient exercise-based cardiac rehabilitation programs with a satisfactory level of baseline functional capacity at the beginning.

The limitations of this study include the lack of long-term follow-up after hospital discharge. Also, the drop-outs exceeded the pre-set allowed percentage for the drop-outs. Nevertheless, this study has several strengths. Our study is one of the few randomised controlled studies in the field of early physical rehabilitation for in-patients with acute HF, which could help future meta-analyses in laying down a foundation for an evidence-based physiotherapy practice for this patient population. Also, in this study, the use of 6-MWT in collaboration with other intermediate endpoints could have produced a consistent evaluation of the clinical benefits of the early mobilisation program in hospitalised HF patients.

Conclusion

An early mobilisation program combined with the usual medical care can help enhance the functional capacity (i.e., ↑ 6-MWD & ↓ RPE score), improve ADL, and reduce the LOS in stabilised patients following acute HF to a greater extent than the usual medical care alone. Early mobilisation could also lead to statistically and clinically meaningful reductions in the NT-proBNP concentrations in these patients if combined with routine medical care. The findings of this study may be of clinical significance for the physiotherapists, physicians, and other health professionals involved in the acute care of hospitalized HF patients. Future research work on this topic may be warranted.

Conflict of Interests

The authors state they have no conflict of interests

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Author Contributions

Ahmad AM has contributed to the concept and the design of the research, the supervision of the research work, the analysis of data and interpretation of the results, writing the whole paper and revising it critically for important intellectual content, ensuring the scientific accuracy and integrity of the paper, the final approval of the paper before submission, and the second revision of the paper as per the reviewers' instructions. Elshenawy AI contributed to the concept and design of the research, application of physiotherapy sessions, evaluation of the outcome measures, data acquisition, as well as the revision and final approval of the paper. Abdelghany M contributed to the concept of the research, the medical supervision of the research work, as well as the revision and final approval of the paper. Abdel-Ghaffar HA contributed to the concept and the design of the research, the supervision of the research work, as well as the revision and the final approval of the paper.

Appendix A

Barthel Index

Activity	Score
Feeding	
	0 = unable
	5 = needshelp cutting, spreading butter, etc. or requires modified diet
	10 = independent
Bathing	
	0 = dependent
	5 = independent (or in shower)
Grooming	
	0 = needs to help with personal care
	5 = independent face/hair/teeth/shaving (implements provided)
Dressing	
	0 = dependent
	5 = needs help but can do about half unaided
	10 = independent (including buttons, zips, laces, etc.)
Bowels	
	0 = incontinent(or needs to be given enemas)
	5 = occasional accident
	10 = continent
Bladder	
	0 = incontinent, or catheterized and unable to manage alone
	5 = occasional accident
	10 = continent
Toilet Use	
	0 = dependent
	5 = needs some help, but can do something alone
	10 = independent (on and off, dressing, wiping)
Transfers (bed to chair and back)	
	0 = unable, no sitting balance
	5 = major help (one or two people, physical), can sit
	10 = minor help (verbal or physical)
	15 = independent
Mobility (on level surfaces)	
	0 = immobile or < 50 yards
	5 = wheelchair independent, including corners, > 50 yards
	10 = walks with help of one person (verbal or physical) > 50 yards
	15 = independent (but may use any aid; for example, stick) > 50 yards
Stairs	
	0 = unable
	5 = needs help (verbal, physical, carrying aid)
	10 = independent
Total (0–100)	
	Higher scores indicate greater functional independence

Source: Mahoney FI, Barthel DW. Functional evaluation: The Barthel index. Md State Med J 1965;14:61–65.

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