European Journal of Preventive Cardiology (2025) **32**, 964–971
https://doi.org/10.1093/eurjpc/zwaf069

FULL RESEARCH PAPER
Cardiac rehabilitation

Association of pre-admission exercise habit with post-discharge outcomes for older patients with heart failure

Taisuke Nakade [1], Daichi Maeda[1]*, Yuya Matsue [1]*, Nobuyuki Kagiyama[1,2], Yudai Fujimoto[1], Tsutomu Sunayama[1], Taishi Dotare[1], Kentaro Jujo [3], Kazuya Saito[4], Kentaro Kamiya[5], Hiroshi Saito [6], Yuki Ogasahara[7], Emi Maekawa [8], Masaaki Konishi [9], Takeshi Kitai[10], Kentaro Iwata[11], Hiroshi Wada[12], Takatoshi Kasai [1,13], Hirofumi Nagamatsu[14], Shin-ichi Momomura[15], and Tohru Minamino[1,16]

[1]Department of Cardiovascular Biology and Medicine, Juntendo University Graduate School of Medicine, 2-1-1 Hongo, Bunkyo-ku, Tokyo 113-8421, Japan; [2]Department of Cardiology, The Sakakibara Heart Institute of Okayama, 2-5-1 Nakaimachi, Kita-ku, Okayama City, Okayama 700-0804, Japan; [3]Department of Cardiology, Nishiarai Heart Centre Hospital, 1-12-8 Nishiaraihommachi, Adachi-ku, Tokyo 123-0845, Japan; [4]Department of Rehabilitation, The Sakakibara Heart Institute of Okayama, 2-5-1 Nakaimachi, Kita-ku, Okayama City, Okayama 700-0804, Japan; [5]Department of Rehabilitation, School of Allied Health Sciences, Kitasato University, 1-15-1 Kitazato, Minami-ku, Sagamihara City, Kanagawa 252-0329, Japan; [6]Department of Rehabilitation, Kameda Medical Centre, 929 Higashimachi, Kamogawa City, Chiba 296-0041, Japan; [7]Department of Nursing, The Sakakibara Heart Institute of Okayama, 2-5-1 Nakaimachi, Kita-ku, Okayama City, Okayama 700-0804, Japan; [8]Department of Cardiovascular Medicine, Kitasato University School of Medicine, 1-15-1 Kitazato, Minami-ku, Sagamihara City, Kanagawa 252-0329, Japan; [9]Division of Cardiology, Yokohama City University Medical Centre, 3-9 Fukura, Kanazawa-ku, Yokohama City, Kanagawa 236-0004, Japan; [10]Department of Cardiovascular Medicine, National Cerebral and Cardiovascular Centre, 6-1 Kishibenishincho, Suita City, Osaka 564-8565, Japan; [11]Department of Rehabilitation, Kobe City Medical Centre General Hospital, 1-1 Minatojimanaka-machi 2-chome, Chuo-ku, Kobe City, Hyogo 650-0047, Japan; [12]Department of Cardiovascular Medicine, Saitama Medical Centre, Jichi Medical University, 847 Amanuma-cho 1-chome, Omiya-ku, Saitama City, Saitama 330-8503, Japan; [13]Cardiovascular Respiratory Sleep Medicine, Juntendo University Graduate School of Medicine, 2-1-1 Hongo, Bunkyo-ku, Tokyo 113-8421, Japan; [14]Department of Cardiology, Tokai University School of Medicine, 143 Shimogasuya, Isehara City, Kanagawa 259-1193, Japan; [15]Department of Medicine, Saitama Citizens Medical Centre, 299-1 Shimane, Nishi-ku, Saitama City, Saitama 331-0054, Japan; and [16]Japan Agency for Medical Research and Development-Core Research for Evolutionary Medical Science and Technology (AMED-CREST), 1-7-1 Otemachi, Chiyoda-ku, Tokyo 100-0004, Japan

Received 26 August 2024; revised 25 November 2024; accepted 24 January 2025; online publish-ahead-of-print 19 February 2025

Aims The benefits of exercise in patients with heart failure are well documented. However, to date, the association between exercise habits and prognosis is yet to be evaluated. In this study, we investigated the association between pre-hospital exercise habits and post-discharge prognosis in older adult patients with heart failure.

Methods and results This *post hoc* analysis utilized data from the FRAGILE-HF study, which included 1262 patients aged ≥ 65 years who required hospitalization for heart failure decompensation. Exercise habits before hospitalization were assessed through a three-question physical activity assessment tool. The primary outcome was all-cause mortality. Of the 1262 patients, 587 (46.5%) reported no regular exercise habits before hospitalization. No significant differences were observed in the histories of heart failure hospitalizations or other comorbidities. However, patients in the exercise habit group consistently exhibited better physical function, such as greater grip strength, gait speed, and short physical performance battery scores, than those in the non-exercise habit group. In addition to physical function, patients with exercise habits exhibited significantly lower all-cause mortality than those without exercise habits (log-rank test, $P = 0.019$). The adjusted Cox regression models suggested that pre-hospital exercise was associated with a lower mortality risk (hazard ratio, 0.75; 95% confidence interval, 0.58–0.98; $P = 0.035$).

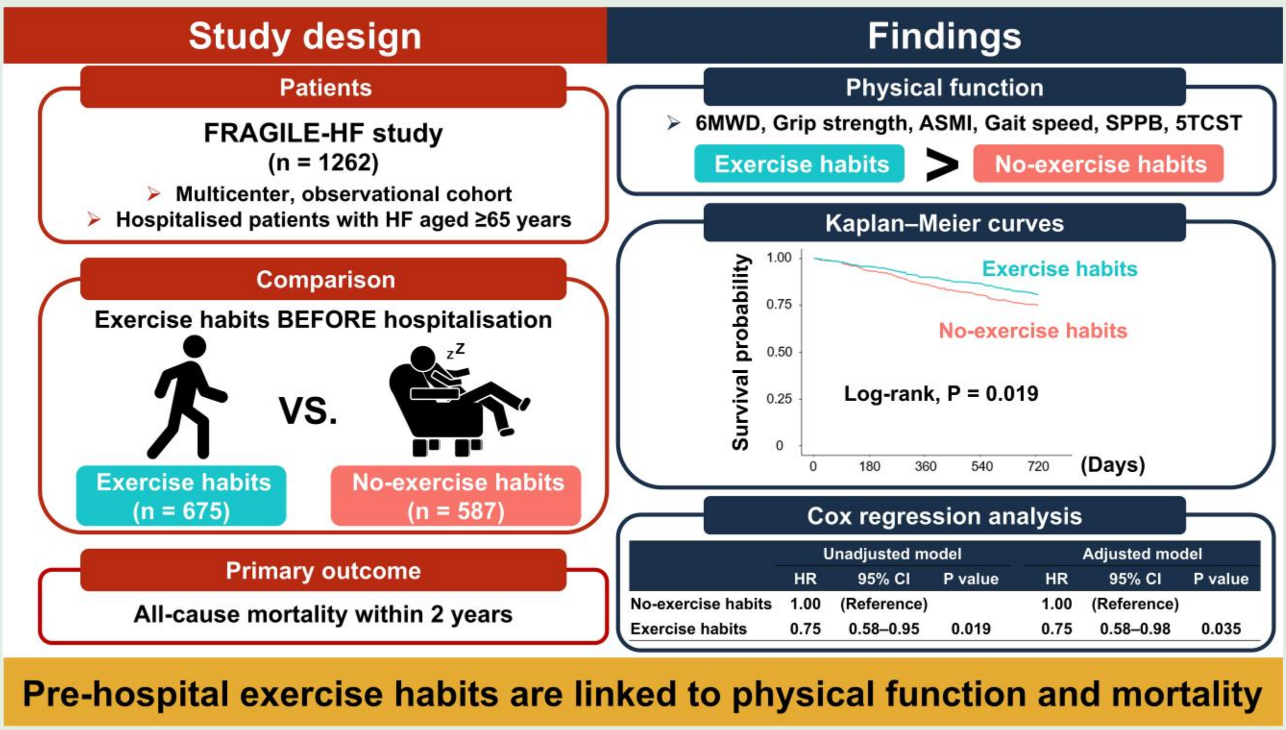
Conclusion Exercise habits before hospitalization were significantly associated with better strength and physical function and lower post-discharge all-cause mortality in older adult patients with heart failure. These findings highlight the importance of assessing exercise habits for risk stratification among this population.

* Corresponding author. Tel: +81 3 3813 3111, Fax: +81 3 5689 0627, Email: daichimaeda0424@yahoo.co.jp (D.M.); Tel: +81 3 3813 3111, Fax: +81 3 5689 0627, Email: yuya8950@gmail.com (Y.M.)

Lay summary This study explored the association of exercise habits before hospital admission on the long-term post-discharge outcomes of older patients with heart failure.

- Older patients with heart failure who maintained regular exercise habits before hospitalization had better physical function at discharge than those who did not exercise.
- These patients also had a significantly lower risk of death within 2 years post-discharge.

Graphical Abstract



Keywords Heart failure • Exercise • Habit • Prognosis • Physical activity

Introduction

The global population is aging, and the prevalence of lifestyle-related diseases is increasing. Thus, heart failure is becoming more common worldwide.[1,2] This condition significantly increases mortality rates and contributes to frequent hospital readmissions, severely impacting the quality of life of those affected.[3,4]

Physical activity, defined as any movement that expends energy beyond resting levels, spans a range of activities, including work, household chores, leisure, transport, sports, and structured exercise.[5] Exercise, a planned, structured, and repetitive form of physical activity, is specifically designed to improve or maintain physical fitness.[5] Exercise therapy for patients with heart failure has demonstrated notable efficacy, particularly in those with reduced ejection fraction.[6,7] In recent years, growing evidence has also highlighted its effectiveness in patients with heart failure with preserved ejection fraction.[8,9] Therefore, exercise-based cardiac rehabilitation is recommended for all stable patients with heart failure to improve their exercise capacity and quality of life and reduce hospital readmissions. The American Heart Association/American College of Cardiology/Heart Failure Society of America and the European Society of Cardiology endorsed this approach as a Class I Level A recommendation.[10–12]

Current guidelines rely heavily on studies that introduce exercise therapy after a heart failure diagnosis. However, there is a noticeable lack of research on the impact of physical activity, including habitual exercise before hospitalization, on post-discharge outcomes. We aimed to explore how pre-hospital exercise habits are associated with the post-discharge prognosis of older adult patients with heart failure using comprehensive data from a multicentre registry.

Methods

Study design and patient cohort

This study included a *post hoc* sub-analysis of data from the FRAGILE-HF study, a prospective, multicentre, observational study conducted at 15 hospitals (eight university hospitals and seven non-university teaching hospitals) in Japan. A comprehensive description and the primary results of this study have been previously published.[13–18] In brief, all consecutive patients aged ≥ 65 years hospitalized for heart failure decompensation and capable of ambulation were assessed for eligibility from September 2016 to March 2018. Heart failure decompensation was diagnosed according to the Framingham criteria.[19]

We excluded patients with (1) a history of heart transplantation or current use of a left ventricular assist device, (2) undergoing chronic peritoneal dialysis or haemodialysis, (3) acute myocarditis, (4) missing data on brain natriuretic peptide (BNP) or n-terminal pro-BNP, and (5) BNP level < 100 pg/mL or n-terminal pro-BNP level < 300 pg/mL upon admission.

Physical examinations, echocardiography, and blood samples were collected under stable conditions before discharge.

The study protocol adhered to the principles of the Declaration of Helsinki and was approved by the ethics committee or institutional review board of the 15 participating hospitals (UMIN000023929). Since this was an observational study without invasive procedures or interventions, written informed consent was deemed unnecessary under the Ethical Guidelines for Medical and Health Research Involving Human Subjects of the Japanese Ministry of Health, Labour, and Welfare. Participants were allowed to withdraw from the study at any time. Information about the study, including its objectives, inclusion and exclusion criteria, and names of the participating institutions, was made available on the University Hospital Information Network before patient enrolment (UMIN-CTR; unique identifier: UMIN000023929).

Exercise habit assessment

Patients' exercise habits before admission to the hospital were assessed using questions based on the three-question physical activity assessment tool developed for use during routine medical consultations. This tool has demonstrated a correlation with the accelerometer-based physical activity levels in a previous study, allowing for a quick and practical assessment suitable for clinical settings.[20] This instrument measured the number of bouts of vigorous-intensity activity that lasted 20 min and bouts of walking or moderate-intensity activity that lasted 30 min in a usual week. Specifically, the responses that indicated a positive exercise habit were (1) How many days a week did you go for a walk lasting >30 min? (encompasses walking and using it as a means of transport to a destination); (2) How many days a week did you undertake at least 30 min of moderate exercise that increased your heart rate or made you feel light-headed or short of breath? (examples include carrying light loads, regular cycling, playing double tennis.); and (3) How many days per week did you perform 20 min or more of vigorous exercise that caused you to sweat or become short of breath? (activities such as jogging and serious cycling). The study population was divided into two groups: the exercise habit group, for those who answered yes and 'at least once daily per week' to any of these questions, and the no-exercise habit group, for those who answered no to all these questions. Total activity was defined using the following formula: total activity (sessions/week) = walking or moderate sessions/week + (2 × vigorous sessions/week).[20]

Muscle mass assessment

We evaluated the association between exercise habits and muscle mass. Muscle mass was assessed using bioelectrical impedance analysis (BC-622; Tanita, Tokyo, Japan), specifically targeting appendicular skeletal muscle mass. The appendicular skeletal muscle mass index was calculated by dividing the total muscle mass in the limbs by the square of the height and was expressed in kg/m^2.

Follow-up and study outcome

The primary outcome of the study was mortality over 2 years. A prospective assessment of the patient's prognosis was performed for 2 years post-discharge until March 2020. After discharge, most patients were followed up in outpatient clinics, and their prognostic information was derived from each hospital's medical records. For patients lacking follow-up data at their respective hospital outpatient clinics, prognostic details were obtained through telephone interviews with family members.

Statistical methods

We assessed the distribution of each continuous variable for normality through a visual inspection of its distribution. Continuous variables are presented as means ± standard deviation or medians with interquartile ranges (IQR). Variables were log-transformed for subsequent analyses, where necessary. Categorical variables are expressed as counts and percentages. The baseline characteristics of patients were compared using the Mann–Whitney *U* test for continuous variables and the χ^2 test for categorical variables, where appropriate. Kaplan–Meier survival curves were drawn, and differences in mortality were analysed using log-rank tests to determine the significance. Hazard ratios (HRs) were calculated using Cox regression analysis, and the prognostic significance of exercise and non-exercise habits was assessed using 95% confidence intervals (CIs). The adjusted factors in the multivariate Cox model for 2-year mortality included the Meta-analysis Global Group in Chronic Heart Failure (MAGGIC) risk score and log-transformed BNP levels. The MAGGIC risk score has been validated as a predictor of mortality in patients with heart failure[21] and including BNP values enhanced the precision of mortality prediction among Japanese patients.[22] The proportional hazards assumption for the Cox regression model was assessed through a visual inspection of Schoenfeld residual plots. The univariate HR for 2-year all-cause mortality was evaluated using a non-linear model with restricted cubic splines to elucidate the association of total activity with mortality. The cubic spline functions were smoothed using 3 degrees of freedom to capture potential non-linear trends. Predicted HRs with 95% CIs were extracted from the model and plotted as a function of total activity. The relationships between the variables were analysed using Path analysis.[23] Path analysis, an extension of regression modelling, is a statistical technique that assesses relationships among multiple variables, illustrating pathways for the hypotheses set by the researcher. This analysis provides a comprehensive view of how predictor variables relate to dependent variables, particularly examining how exercise habits, comorbidities, and frailty, as assessed by the Frailty score,[24] interact to influence the primary outcome. Reportedly, unstandardized and standardized effect sizes convey the strength of these relationships. Unstandardized coefficients retain the original measurement scale of each variable, emphasizing the strength of associations between variables. In contrast, standardized coefficients convert values into a common unit, enabling comparison of each variable's effect on the outcome. Model adequacy was tested using the relative chi-square (χ^2/df) and root mean square error of approximation (RMSEA), with model fit considered acceptable when the RMSEA was < 0.10 and the χ^2/df ratio fell between 1 and 5. Path analysis was conducted using the lavaan package in R Studio (version 4.2.2, R Foundation for Statistical Computing, Vienna, Austria), with path diagrams visualized using the semPlot package. Statistical significance was determined using a two-tailed *P*-value of < 0.05. All analyses were conducted using the R Studio statistical software, version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Study population and classification

Initially, 1332 inpatients were enrolled in the FRAGILE-HF study. Of these, 70 were excluded due to the absence of a completed questionnaire. Consequently, 1262 patients [median age, 81 (IQR, 74–86) years; 43.1% female] were included in the analysis. The participants were classified into four groups based on the highest reported exercise intensity before hospitalization. Further analysis revealed that 296 participants (23.5%) were categorized as engaging in walking exercise, 163 (12.9%) reported moderate-intensity exercise, and 216 (17.1%) engaged in vigorous-intensity exercise, while 587 participants (46.5%) reported no exercise habits. Furthermore, 587 (46.5%) and 675 (53.4%) patients were classified into the non-exercise and exercise habit groups, respectively.

Baseline characteristics of the exercise and non-exercise habit groups

Table 1 presents a comparison of baseline characteristics between the two groups. The exercise habit group was younger and had a larger

Table 1 Participants' baseline characteristics

Variables	No-exercise habit $n = 587$	Exercise habit $n = 675$	*P* value	Missing rate (%)
Age (years)	82 [76–87]	80 [73–85]	<0.001	0.0
Male sex (%)	296 (50.4)	422 (62.5)	<0.001	0.0
NYHA class III/IV (%)	98 (16.7)	80 (11.9)	0.013	0.0
BMI (kg/m^2)	21.1 ± 4.0	21.7 ± 3.6	0.009	0.4
SBP (mm Hg)	113.3 ± 16.8	114.0 ± 17.3	0.466	0.0
DBP (mm Hg)	62.2 ± 11.2	62.0 ± 10.2	0.735	0.0
Heart rate (beats/min)	72.0 ± 14.1	70.1 ± 13.6	0.015	0.0
LVEF (%)	47.3 ± 16.9	44.8 ± 16.5	0.010	1.1
History of heart failure (%)			0.221	0.2
De novo	91 (15.5)	103 (15.3)		
Less than 1.5 years	247 (42.1)	254 (37.7)		
Equal/more than 1.5 years	249 (42.4)	317 (47.0)		
Comorbidities (%)				
Hypertension	415 (70.7)	482 (71.4)	0.804	0.0
Diabetes	203 (34.6)	245 (36.3)	0.555	0.0
Atrial fibrillation	269 (45.8)	290 (43.0)	0.334	0.0
COPD	64 (10.9)	72 (10.7)	0.928	0.0
Coronary artery disease	212 (36.1)	237 (35.1)	0.724	0.0
TIA/stroke	87 (14.8)	81 (12.0)	0.165	0.0
Frailty score	3 (2–3)	2 (1–3)	<0.001	8.0
Prescription at discharge (%)				
Loop diuretics	525 (89.4)	575 (85.2)	0.028	0.0
Beta blocker	423 (72.1)	501 (74.2)	0.408	0.0
ACE–I/ARB	373 (63.5)	477 (70.7)	0.008	0.0
MRA	272 (46.3)	346 (51.3)	0.090	0.0
Laboratory data at discharge				
Haemoglobin (g/dL)	11.7 ± 2.0	11.9 ± 2.0	0.011	0.2
Creatinine (mg/dL)	1.14 (0.89–1.60)	1.18 (0.94–1.55)	0.282	0.2
BUN (mg/dL)	27 (20–38)	25 (19–34)	0.028	0.2
Serum sodium (mmol/L)	139.0 ± 3.9	139.0 ± 3.7	0.971	0.2
CRP (mg/dL)	0.30 (0.13–0.92)	0.23 (0.10–0.65)	0.002	2.2
BNP (pg/mL)	284 (146–527)	262 (123–455)	0.049	13.2

Continuous values are presented as medians (interquartile ranges) or means (standard deviations). Categorical variables are expressed as numbers (%).
ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ASMI, appendicular skeletal muscle mass index; BMI, body mass index; BNP, brain natriuretic peptide; BUN, blood urea nitrogen; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; DBP, diastolic blood pressure; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; NYHA, New York Heart Association; SBP, systolic blood pressure; TIA, transient ischaemic attack.

proportion of males and lower C-reactive protein levels. However, no significant differences were observed in the histories of heart hospitalizations, systolic blood pressure, hypertension, or diabetes. *Table 2* compares physical function between the exercise and non-exercise habit groups. The exercise habit group was consistently associated with better physical function, gait speed, five-time chair stand, higher grip strength, and shorter physical performance battery scores than the non-exercise habit group. In addition, males in the exercise habit group had higher appendicular skeletal muscle index than those in the non-exercise habit group. Physical function was also assessed in patients with left ventricular ejection fraction (LVEF) < 50% and in those with LVEF ≥ 50%. All physical functions were significantly higher in those with exercise habits, regardless of whether the LVEF was < 50% or ≥ 50%. The appendicular skeletal muscle index was higher in males with exercise habits only when the LVEF was < 50%. However, consistent with the baseline characteristics, no significant difference was observed in the skeletal muscle index of females regardless of LVEF (see Supporting Information Supplementary material online, *Tables S1* and *S2*).

Association between exercise habit and mortality

During the follow-up, 258 out of the 1262 patients (20.4%) died: 136 (23.2%) and 122 (18.1%) in the non-exercise and exercise habit groups, respectively. The Kaplan–Meier analysis revealed a significant difference between both groups (log-rank test, $P = 0.019$; *Figure 1*).

The proportional hazards assumption for the Cox model was assessed and confirmed to be generally satisfied. The analysis demonstrated that exercise habit remained an independent prognostic factor for all-cause mortality, even after the adjusted model (HR, 0.75; 95% CI, 0.58–0.98; $P = 0.035$; *Table 3*). After adjusting the model,

Table 2 Physical function comparison by exercise habits

Variables	Males				Females			
	No-exercise habit $n = 296$	Exercise habit $n = 422$	*P* value	Missing rate (%)	No-exercise habit $n = 291$	Exercise habit $n = 253$	*P* value	Missing rate (%)
ASMI (kg/m²)	7.32 (6.61–8.44)	7.71 (6.87–8.52)	0.039	31.7	6.51 (5.95–7.09)	6.45 (5.84–7.04)	0.398	33.4
Grip strength (kg)	22.2 (18.5–26.7)	24.9 (21.0–30.5)	<0.001	2.8	13.0 (9.9–16.1)	15.0 (12.2–18.3)	<0.001	3.7
Physical performance								
Gait speed (m/s)	0.78 (0.59–0.97)	0.90 (0.71–1.09)	<0.001	2.6	0.58 (0.43–0.79)	0.76 (0.58–0.94)	<0.001	2.6
5-time chair–stand test (s)	13.5 (10.4–17.2)	11.4 (9.1–15.0)	<0.001	17.8	16.0 (11.8–21.5)	13.0 (10.4–16.5)	<0.001	26.8
SPPB	8 (6–11)	10 (8–12)	<0.001	4.2	6 (4–9)	9 (6–11)	<0.001	3.3
6MWD (m)	232 (150–338)	319 (220–395)	<0.001	7.8	160 (86–240)	240 (180–340)	<0.001	9.8

Values are presented as the median (interquartile range).
6MWD, 6-minute walk distance; ASMI, appendicular skeletal muscle mass index; SPPB, short physical performance battery.

no significant interaction was observed between LVEF < 50% and ≥ 50% regarding the prognostic impact of exercise habits (*P* for interaction = 0.94). As a sensitivity analysis, we performed the same Cox proportional hazards analysis on a population excluding patients who died within the first year ($n = 147$) and found consistent results even though it was not statistically significant (adjusted HR, 0.80; 95% CI, 0.54–1.21; $P = 0.298$). In addition, a non-linear model using restricted cubic splines demonstrated that the HR plateaued when total activity exceeded approximately 1–2 sessions weekly, aligning with the patterns observed in previous analyses (*Figure 2*).

Similar analyses stratified by exercise intensity, including Kaplan–Meier and Cox proportional hazards analyses, revealed a statistically significant difference in the 2-year mortality across the groups (log-rank test, $P = 0.013$). In the Cox proportional hazards analysis, there was a stepwise decrease in HR across walking, moderate, and vigorous exercise intensities. However, none was statistically significant in the multivariate model (see Supplementary material online, *Figure S1* and *Table S3*).

The path analysis model (see Supplementary material online, *Figure S2*) illustrates the hypothesized relationships between exercise habits, frailty, comorbidities, and 2-year mortality. This model demonstrated an excellent fit with the data, as indicated by an RMSEA of 0.000 and the Comparative Fit and Tucker-Lewis Indices at 1.000. Parameter estimates from the path analysis are detailed in Supplementary material online, *Table S4*. Exercise habit demonstrated a statistically significant negative association with 2-year mortality ($\beta = -0.050$, $P = 0.035$), whereas frailty did not reach statistical significance. Furthermore, the analysis revealed contrasting associations for other comorbidities: hypertension showed a positive association with 2-year mortality ($\beta = 0.085$, $P = 0.022$), while chronic obstructive pulmonary disease (COPD) exhibited a negative association ($\beta = -0.059$, $P = 0.024$).

Discussion

This retrospective analysis of the FRAGILE-HF registry data offered insights into the prognostic importance of exercise habits before hospitalization in older adult patients hospitalized for heart failure. Our results indicated that over 50% of the study cohort, comprising older adult patients hospitalized with heart failure, did not participate in any exercise before hospitalization. Those who exercised before hospitalization had better physical function as measured before discharge. Moreover, exercise habits were significantly associated with a lower risk of all-cause mortality independent of conventional risk factors. These results suggest that exercise habits, after discharge and before hospitalization, may be associated with a better prognosis.

Frequency of exercise habits before hospitalization

Notably, many studies have examined the benefits of exercise for patients with heart failure. However, most have focused on activities that started after heart failure admission. For example, a survey by Kamiya et al., which included 270 institutions, found that only 7% (3741 of 51 323) of those hospitalized with heart failure underwent cardiac rehabilitation after discharge.[25] Hence, details regarding exercise frequency before hospitalization for heart failure are limited. Nevertheless, data from the first National Health and Nutrition Examination Survey (NHANES I) Epidemiologic Follow-up Study, a prospective cohort analysis of NHANES I participants aged 25–74 years during the 1971–1975 survey period, sought to investigate the link between physical inactivity and chronic heart failure (incident heart failure determined by one or more hospital or nursing home admissions).[26] This study found that physical inactivity was reported by 44.1% of participants.[26] In contrast, our data showed that approximately 50% of participants had no exercise habits. This differs from the two cohort studies (those with no history of heart failure in NHANES I and those hospitalized for heart failure in FRAGILE-HF) as well as the age and definition of physical activity. However, the frequency of inactivity is consistent. This consistency may support the validity of our analysis.

Prognostic impact of physical activity in older adult patients with heart failure

Physical activity is critically important for people of all ages looking to improve their health.[27] Focusing on the incidence of heart failure, Pandey *et al*. conducted a comprehensive meta-analysis using data from 12 prospective cohort studies. They confirmed a clear, linear, and inverse relationship between physical activity and the risk of developing heart failure.[28] As for the impact of exercise on outcomes for those diagnosed with heart failure, Doukky *et al*.[29] analysed 902 patients with heart failure classified as New York Heart Association class II/III and found that physical inactivity significantly increased the future risk of all-cause mortality and cardiac death.

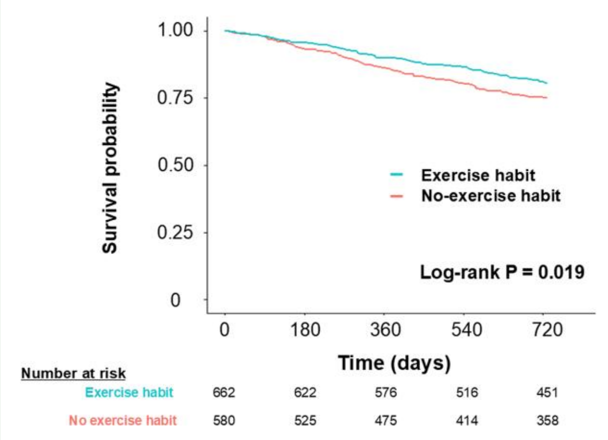


Figure 1 Kaplan–Meier curves for the primary outcome based on exercise habit. The figure displays Kaplan–Meier curves illustrating the 2-year mortality rates among two groups: individuals with and without a positive exercise habit.

Table 3 Cox proportional hazards analysis of exercise habits for 2-year mortality

	Unadjusted model			Adjusted model[a]		
	HR	95% CI	*P* value	HR	95% CI	*P* value
No exercise habits	1.00	(Reference)		1.00	(Reference)	
Exercise habits	0.75	0.58–0.95	0.019	0.75	0.58–0.98	0.035

[a]Adjusted for the Meta-analysis Global Group in Chronic Heart Failure risk score and log-transformed brain natriuretic peptide.
CI, confidence interval; HR, hazard ratio.

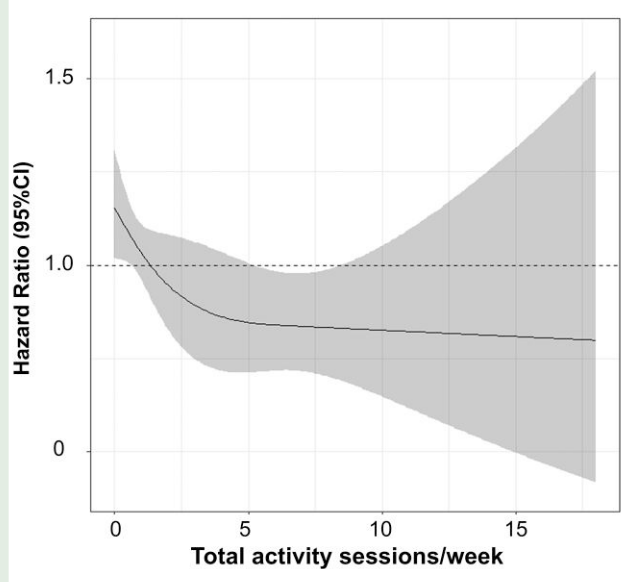


Figure 2 Association between 2-year mortality and total activity (sessions/week) evaluated using restricted cubic splines. The analysis demonstrates that the risk of mortality plateaus when total activity exceeds 1–2 sessions/week. CI, confidence interval.

These results are in line with ours and show that physical inactivity is associated with adverse events in patients with heart failure. Furthermore, when examining whether exercise habits were dose-dependent, the HR reached a relative plateau with further increases in total activity, provided that exercise was performed more than once or twice weekly. This finding is also consistent with previous studies on daily step counts, which demonstrated a dose–response pattern where the effect stabilizes beyond a certain threshold.[30–32]

Our study provided several novel findings. First, patients with pre-hospitalization exercise habits were associated with a favourable post-discharge prognosis. Second, exercise habits were associated with greater physical function before discharge, even among hospitalized patients with heart failure. Third, our results may expand previous findings on the favourable association between exercise habits and prognosis in older adult patients with heart failure, given the median age of our study cohort (82 vs. 80 years for the non-exercise vs. exercise habit group, respectively). Finally, our results suggested the validity of the simple questionnaire on exercise habits used in this study, considering its association with physical function and post-discharge prognosis in older adult patients with heart failure.

However, our study was not designed to elucidate the association between pre-hospitalization exercise habits and post-discharge prognosis. The reasons might be better physical function achieved before hospitalization, prolonged exercise habits even after discharge in those with exercise habits before admission, or both. Further research is required to clarify this point.

Limitations

This study had several limitations. This study was a *post hoc* analysis of a prospective observational cohort study inherently subject to certain constraints. Despite adjusting for covariates, negating the influence of measured and unmeasured confounders was impossible. We adjusted for covariates such as the MAGGIC risk score, which includes comorbidities like COPD and hypertension; however, it remains possible that patients with pre-hospital exercise habits were in better general health at baseline and had fewer complications. These factors may have independently influenced the observed outcomes, introducing the potential for ascertainment bias. To address this concern, we used path analysis, which identified associations between exercise habits and prognosis with statistical significance. Path analysis is a valuable tool for examining complex relationships and understanding the interplay of variables; however, it does not provide definitive evidence of causation. Therefore, our findings should be interpreted with caution, as they offer insights into possible pathways but cannot fully establish direct relationships. Additional studies employing methodologies specifically designed to confirm these associations are necessary to validate these results. These further investigations would provide a clearer understanding of the relationship between exercise habits and prognosis in older patients with heart failure. Furthermore, relying on questionnaires to assess exercise habits introduces subjectivity and lacks objective verification using devices such as activity metres or accelerometres. Self-reported data inherently carry the risk of recall bias and social desirability bias, which may affect the accuracy of the responses. These biases could lead participants to overestimate their exercise habits or misremember their actual activity levels. Nevertheless, the results lend validity to the questionnaire as a practical tool. Participants who reported exercise habits before hospitalization had significantly better physical function outcomes at discharge—including higher 6-min walk distances and grip strength than those without exercise habits. This suggests that despite its limitations, the questionnaire captured meaningful differences in physical activity. The exercise habits were assessed once at the initial admission, without further follow-up, to observe post-discharge changes. Excluding some patients due to the absence of data on exercise habits could have introduced a selection bias, potentially distorting the outcomes.

The relatively short 2-year follow-up period may also limit the ability to evaluate long-term outcomes. This duration may not fully capture the late association of exercise habits with mortality, highlighting the need for further studies with longer follow-up periods. In addition, the BNP levels in our cohort were relatively low compared with those typically observed in older patients with decompensated heart failure. This is likely due to the timing of blood sample collection, which was conducted just before discharge after patients had already received hospital-based treatment and were in a more stable clinical state. Furthermore, longer hospital stays in Japan, as seen in the nationwide registry, are generally associated with more stable BNP levels at discharge, which may be a contributing factor.[1] Therefore, the BNP levels in this study may not fully reflect the broader population of patients with heart failure, especially those in outpatient settings, where BNP levels are generally higher. This study focused solely on older adult patients with heart failure in Japan, highlighting the need for further studies with younger groups or populations from Western countries.

In conclusion, older adult patients with a pre-hospitalization exercise routine admitted to hospital for heart failure exhibited better physical function and lower all-cause mortality post-discharge compared to those without such a routine. Further research is warranted to determine how exercise habits before admission influence lifestyle, exercise behaviour, and prognosis after discharge.

Supplementary material

Supplementary material is available at *European Journal of Preventive Cardiology*.

Acknowledgements

We acknowledge that no artificial intelligence programs, such as ChatGPT or similar software, were used to compile the submitted manuscript. Therefore, there are no declarations regarding the use of artificial intelligence.

Author contribution

T.N., D.M., and Y.M. contributed to the conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, software, and writing of the original draft. Y.M. contributed to funding acquisition and supervision. All authors revised the manuscript, approved the final manuscript, and agreed to be accountable for all aspects of the work, ensuring its integrity and accuracy.

Funding

FRAGILE-HF was supported by Novartis Pharma Research Grants and a Japan Heart Foundation Research Grant. This research was funded by Japan Agency for Medical Research and Development (AMED) under grant number JP21ek0109543.

Conflict of interest: N.K. is affiliated with a department funded by Paramount Bed Co., Ltd., based on collaborative research agreements and received honoraria from Novartis Japan, Otsuka Pharmaceutical Co., Ltd., Nippon Boehringer Ingelheim Co., Ltd., Eli Lilly Japan, AstraZeneca, AMI Inc., and EchoNous. K.K. received funding outside the submitted work from Eiken Chemical Co., Ltd. and SoftBank Corporation, Ltd. T.K. is affiliated with a department sponsored by Philips Unk Onics, ResMed, Teijin Home Healthcare, and Fukuda Denshi. Y.M. received honoraria from Otsuka Pharmaceutical Co., EN Otsuka Pharmaceutical Co., Ltd., Novartis Pharma K.K., Bayer Inc., and AstraZeneca, and a collaborative research grant from Pfizer Japan Inc., Otsuka Pharmaceutical Co., EN Otsuka Pharmaceutical Co., Ltd., Nippon Boehringer Ingelheim Co., Ltd., Roche Diagnostics International Ltd., and Roche Diagnostics K.K.

Data availability

Data supporting the findings of this study are available from the corresponding author (Y.M.) upon reasonable request.

References

1. Ambrosy AP, Fonarow GC, Butler J, Chioncel O, Greene SJ, Vaduganathan M, *et al.* The global health and economic burden of hospitalizations for heart failure: lessons learned from hospitalized heart failure registries. *J Am Coll Cardiol* 2014;**63**:1123–1133.
2. Ohira T, Eguchi E, Hayashi F, Kinuta M, Imano H. Epidemiology of cardiovascular disease in Japan: an overview study. *J Cardiol* 2024;**83**:191–200.
3. McMurray JJ, Pfeffer MA. Heart failure. *Lancet* 2005;**365**:1877–1889.
4. Saku K, Yokota S, Nishikawa T, Kinugawa K. Interventional heart failure therapy: a new concept fighting against heart failure. *J Cardiol* 2022;**80**:101–109.
5. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Rep* 1985; **100**:126–131.
6. Okamura M, Kataoka Y, Taito S, Fujiwara T, Ide A, Oritsu H, *et al.* Early mobilization for acute heart failure: a scoping and a systematic review. *J Cardiol* 2024;**83**:91–99.
7. Noda T, Kamiya K, Hamazaki N, Nozaki K, Uchida S, Ueno K, *et al.* Effect of change in hepato-renal function and cardiac rehabilitation on mortality in patients with heart failure. *J Cardiol* 2024;**84**:355–361.
8. Dibben GO, Hannay JR, Taylor RS. Exercise training in heart failure. *Heart* 2024;**110**: 373–381.
9. Sachdev V, Sharma K, Keteyian SJ, Alcain CF, Desvigne-Nickens P, Fleg JL, *et al.* Supervised exercise training for chronic heart failure with preserved ejection fraction: a scientific statement from the American Heart Association and American College of Cardiology. *Circulation* 2023;**147**:e699–e715.
10. Pelliccia A, Sharma S, Gati S, Bäck M, Börjesson M, Caselli S, *et al.* 2020 ESC guidelines on sports cardiology and exercise in patients with cardiovascular disease. *Eur Heart J* 2021; **42**:17–96.
11. Authors/Task Force M, McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, *et al.* 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: developed by the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). with the special contribution of the heart failure association (HFA) of the ESC. *Eur J Heart Fail* 2022;**24**:4–131.
12. Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, *et al.* 2022 AHA/ ACC/HFSA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association joint committee on clinical practice guidelines. *Circulation* 2022;**145**:e895–e1032.
13. Matsue Y, Kamiya K, Saito H, Saito K, Ogasahara Y, Maekawa E, *et al.* Prevalence and prognostic impact of the coexistence of multiple frailty domains in elderly patients with heart failure: the FRAGILE-HF cohort study. *Eur J Heart Fail* 2020;**22**:2112–2119.
14. Maekawa E, Noda T, Maeda D, Yamashita M, Uchida S, Hamazaki N, *et al.* Prognostic impact of cachexia by multi-assessment in older adults with heart failure: FRAGILE-HF cohort study. *J Cachexia Sarcopenia Muscle* 2023;**14**:2143–2151.
15. Nakade T, Maeda D, Matsue Y, Fujimoto Y, Kagiyama N, Sunayama T, *et al.* Bendopnea prevalence and prognostic value in older patients with heart failure: FRAGILE-HF-SONIC-HF post hoc analysis. *Eur J Prev Cardiol* 2024;**31**:1363–1369.
16. Saito H, Maeda D, Kagiyama N, Sunayama T, Dotare T, Fujimoto Y, *et al.* Prognostic value of objective social isolation and loneliness in older patients with heart failure: subanalysis of FRAGILE-HF and kitasato cohort. *J Am Heart Assoc* 2024;**13**:e032716.
17. Fujimoto Y, Matsue Y, Maeda D, Kagiyama N, Sunayama T, Dotare T, *et al.* Association and prognostic value of multidomain frailty defined by cumulative deficit and phenotype models in patients with heart failure. *Can J Cardiol* 2024;**40**:677–684.
18. Yamashita M, Kamiya K, Hamazaki N, Nozaki K, Saito H, Saito K, *et al.* Work status before admission relates to prognosis in older patients with heart failure partly through social frailty. *J Cardiol* 2022;**79**:439–445.

19. Ho KK, Anderson KM, Kannel WB, Grossman W, Levy D. Survival after the onset of congestive heart failure in Framingham Heart Study subjects. *Circulation* 1993;**88**: 107–115.
20. Smith BJ, Marshall AL, Huang N. Screening for physical activity in family practice: evaluation of two brief assessment tools. *Am J Prev Med* 2005;**29**:256–264.
21. Pocock SJ, Ariti CA, McMurray JJ, Maggioni A, Køber L, Squire IB, *et al.* Predicting survival in heart failure: a risk score based on 39 372 patients from 30 studies. *Eur Heart J* 2013; **34**:1404–1413.
22. Sawano M, Shiraishi Y, Kohsaka S, Nagai T, Goda A, Mizuno A, *et al.* Performance of the MAGGIC heart failure risk score and its modification with the addition of discharge natriuretic peptides. *ESC Heart Fail* 2018;**5**:610–619.
23. Taheri F, Taheri M, Tavasoli S, Basiri A, Borumandnia N. A path analysis to investigate the interaction between serum, urinary and demographic factors influencing urine calcium in kidney stone formers. *Int Urol Nephrol* 2023;**55**:1829–1836.
24. Yamada M, Arai H. Predictive value of frailty scores for healthy life expectancy in community-dwelling older Japanese adults. *J Am Med Dir Assoc* 2015;**16**: 1002.e7–1002.e1011.
25. Kamiya K, Yamamoto T, Tsuchihashi-Makaya M, Ikegame T, Takahashi T, Sato Y, *et al.* Nationwide survey of multidisciplinary care and cardiac rehabilitation for patients with heart failure in Japan- an analysis of the AMED-CHF study. *Circ J* 2019;**83**:1546–1552.
26. He J, Ogden LG, Bazzano LA, Vupputuri S, Loria C, Whelton PK. Risk factors for congestive heart failure in US men and women: NHANES I epidemiologic follow-up study. *Arch Intern Med* 2001;**161**:996–1002.
27. Piercy KL, Troiano RP, Ballard RM, Carlson SA, Fulton JE, Galuska DA, *et al.* The physical activity guidelines for Americans. *JAMA* 2018;**320**:2020–2028.
28. Pandey A, Garg S, Khunger M, Darden D, Ayers C, Kumbhani DJ, *et al.* Dose-response relationship between physical activity and risk of heart failure: a meta-analysis. *Circulation* 2015;**132**:1786–1794.
29. Doukky R, Mangla A, Ibrahim Z, Poulin M-F, Avery E, Collado FM, *et al.* Impact of physical inactivity on mortality in patients with heart failure. *Am J Cardiol* 2016;**117**: 1135–1143.
30. Stens NA, Bakker EA, Manas A, Buffart LM, Ortega FB, Lee D-C, *et al.* Relationship of daily step counts to all-cause mortality and cardiovascular events. *J Am Coll Cardiol* 2023; **82**:1483–1494.
31. Paluch AE, Bajpai S, Bassett DR, Carnethon MR, Ekelund U, Evenson KR, *et al.* Daily steps and all-cause mortality: a meta-analysis of 15 international cohorts. *Lancet Public Health* 2022;**7**:e219–e228.
32. Sheng M, Yang J, Bao M, Chen T, Cai R, Zhang N, *et al.* The relationships between step count and all-cause mortality and cardiovascular events: a dose-response meta-analysis. *J Sport Health Sci* 2021;**10**:620–628.