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Lifestyle Walking Intervention in Patients With Heart Failure With Reduced Ejection Fraction: The WATCHFUL Trial

Running Title: *Vetrovsky et al.; Walking Intervention in Heart Failure*

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Abstract

Background: Physical activity is pivotal in managing heart failure with reduced ejection fraction (HFrEF), and walking integrated into daily life is an especially suitable form of such physical activity. This study aimed to determine if a 6-month lifestyle walking intervention combining self-monitoring and regular phone counseling improves functional capacity assessed by the six-minute walk test (6MWT) in stable patients with HFrEF compared to usual care.

Methods: The WATCHFUL trial was a 6-month, multicenter, parallel-group, randomized, controlled trial recruiting HFrEF patients from six Czech cardiovascular centers. Eligible participants were ≥18 years old with left ventricular ejection fraction <40% and NYHA class II/III symptoms, on guidelines-recommended medication, excluding those exceeding 450m in the baseline 6MWT. Patients in the intervention group were equipped with a Garmin vívofit activity tracker and received monthly phone counseling from research nurses who encouraged them to employ behavior change techniques such as self-monitoring, goal-setting, and action planning to increase their daily step count. The control group patients continued usual care. The primary outcome was the difference between groups in the distance (in meters) walked during the 6MWT at 6 months. Secondary outcomes included daily step count and minutes of moderate-to-vigorous physical activity (MVPA) as measured by the hip-worn Actigraph wGT3X-BT accelerometer, NT-proBNP and hsCRP biomarkers, ejection fraction, anthropometric measures, depression score, self-efficacy, quality of life, and survival risk score. The primary analysis was conducted by intention-to-treat.

Results: From 218 screened patients, 202 were randomized (65 years; 22.8% female; 90.6% NYHA II; left ventricular ejection fraction 32.5%; 6MWT 385m; 5071 steps/day; 10.9 minutes of MVPA per day). At six months, no between-group differences were detected for the 6MWT (7.4 m, 95% CI -8.0 to 22.7, p=0.345, N=186). The intervention group increased their average daily step count by 1420 (95% CI: 749; 2091) and daily minutes of MVPA by 8.2 (95% CI: 3.0; 13.3) over the control group. No between-group differences were detected for any other secondary outcomes.

Conclusions: While the lifestyle intervention in patients with HFrEF improved daily steps by about 25%, it failed to demonstrate a corresponding improvement in functional capacity. Further research is needed to understand the disconnect between increased physical activity and functional outcomes.

Clinical Trial Registration: ClinicalTrials.gov (NCT03041610, https://clinicaltrials.gov/ct2/show/NCT03041610).

Keywords: physical activity; behavior change; activity tracker; Garmin; self-monitoring; phone counseling; functional capacity; six-minute walk test; step count; moderate-to-vigorous physical activity; cardiac rehabilitation

Non-standard Abbreviations and Acronyms

BDI-II: Beck depression inventory-II
GSE: General self-efficacy scale
HFrEF: heart failure with reduced ejection fraction
hsCRP: high-sensitivity C-reactive protein
MAGGIC: Meta-Analysis Global Group in Chronic Heart Failure
MVPA: moderate-to-vigorous physical activity
NT-proBNP: N-terminal pro–B-type natriuretic peptide
PA: physical activity
SAP: statistical analysis plan
SF-36: 36-item short-form health survey
WATCHFUL: Walking in Chronic Heart Failure Trial
6MWT: six-minute walk test

Clinical Perspective

What is new?

- A simple lifestyle walking intervention, combining self-monitoring with an activity tracker and phone counseling, can increase daily step count of heart failure patients by approximately 25%.
- The intensity of lifestyle walking interventions may not be sufficient to elicit improvements in the functional capacity of patients with heart failure with reduced ejection fraction.

What are the clinical implications?

- Traditional supervised, structured exercise-based cardiac rehabilitation programs continue to be the standard strategy for improving functional capacity, quality of life, and prognosis in patients with heart failure with reduced ejection fraction.
- These programs can be supplemented with simple lifestyle physical activity interventions, utilizing tools such as activity trackers, to support long-term behavioral change and enhance health outcomes.

Introduction

Heart failure with reduced ejection fraction (HFrEF) represents a substantial burden on global health, contributing significantly to hospital admissions, healthcare costs, and mortality.[1] Physical activity (PA) and exercise are fundamental in managing HFrEF, with potential benefits in improving functional capacity and quality of life and enhancing patient prognosis.[2–5] However, the optimal strategy to increase PA in this population remains elusive.[6]

While traditional supervised, structured exercise-based cardiac rehabilitation programs have demonstrated benefits,[7,8] their availability and accessibility are often limited, reaching only a fraction of eligible patients.[9,10] Additionally, the demanding intensity of the exercises, logistical issues such as transportation difficulties and inconvenient scheduling, and individual time constraints contribute to lower adherence rates.[11,12] Lastly, these programs often fail to induce sustained behavioral change, resulting in their impact being frequently short-term.[13]

In contrast, lifestyle PA interventions have emerged as an alternative approach.[14] These interventions aim to seamlessly integrate increased PA levels into daily life, often promoting walking as a natural, accessible form of exercise.[15] By focusing on incorporating walking into everyday routines, lifestyle walking interventions offer a more flexible and sustainable solution, potentially addressing the limitations associated with more structured programs.[16] Typically, these interventions employ various behavior change techniques such as goal setting, action planning, and self-monitoring.[13] They commonly utilize activity trackers to facilitate self-monitoring and often combine this technology with human support, i.e., phone counseling, to enhance adherence and effectiveness.[17,18] Prior research involving patients with conditions like chronic respiratory diseases, cardiovascular diseases, or type 2 diabetes

has shown that similar interventions can result in substantial step count increases ranging from 1,000 to 2,000 steps daily.[17,19–23] Moreover, these step count increments have been linked to significant health benefits, including reduced systolic blood pressure, decreased waist circumference, and lowered low-density lipoprotein cholesterol levels, as well as enhanced functional capacity.[16,23–25]

Yet, whether lifestyle walking interventions can attain a substantial step count increase among patients with HFrEF and whether such increases transform into enhanced functional capacity remains unexplored.[26] The WAlking in Chronic Heart FailUre (WATCHFUL) trial aimed to address this gap by investigating whether a 6-month lifestyle walking intervention, compared to usual care, can elicit improvements in 6-minute walk test (6MWT) distance, a measure of functional capacity, in stable HFrEF patients.

Methods

Trial Design

The WATCHFUL trial was a 6-month, multicenter, parallel-group, randomized, controlled trial performed from August 2018 to June 2023 at six clinical centers in the Czech Republic, of which four were tertiary cardiovascular centers, one regional cardiovascular center, and one large outpatient ambulatory center, all providing specialized outpatient heart failure services (e-Appendix 1). The trial protocol received approval from the multicenter Ethics Committee of the General University Hospital in Prague (20/16 Grant VES 2017 AZV VFN) and has been registered at ClinicalTrials.gov, NCT03041610. The trial protocol and statistical analysis plan (SAP) have been published in detail elsewhere.[27,28] Details regarding the deviations from the published protocol can be found in e-Appendix 2. The data that support the findings of this study are available from the corresponding author upon reasonable request (e-Appendix 3).

Participants

The trial recruited patients aged ≥18 years with stable HFrEF (left ventricular ejection fraction <40%) and New York Heart Association (NYHA) class II or III symptoms, on evidence-based medication with maximally tolerated dosages. We excluded patients who had signs or symptoms of decompensated heart failure, uncontrolled arrhythmia or effort-induced angina, severe or symptomatic aortic stenosis, persistent hypotension, and recent events (<3 months) such as myocardial infarction, percutaneous coronary intervention, implantation of an implantable cardioverter defibrillator or bi-ventricular pacemaker or shocks delivered by the automated implantable cardioverter defibrillator. Potential participants were screened using the 6MWT and those exceeding 450 m or unable to complete the test were excluded. For the full set of inclusion and exclusion criteria, see e-Appendix 4.

Sample Size

To detect a clinically meaningful change of 45 m on the 6MWT[29] with 80% power using a two-sided 0.05 significance level (alpha) and assuming a standard deviation of within-group change of 100 m, 79 participants were required in each group. Anticipating an attrition rate of 20%, our recruitment goal was set at 100 patients per group, leading to a total of 200 patients. The clinically meaningful change of 45 m was derived from the work of Shoemaker et al., who triangulated the minimum clinically meaningful difference using various methods of analyzing existing data.[29] The standard deviation for within-group change, set at 100 m, was based on findings from previous studies.[29–31]

Randomization and Blinding

Patients were randomized in a 1:1 ratio to either the intervention or control group. Centralized randomization was executed using a computer-automated system to ensure proper allocation concealment. The trial employed a permuted block randomization scheme, stratified by center, NYHA class, sex, and age (18–65, ≥66) to guarantee balanced group

representation.

Given the trial's design, blinding of patients and researchers was not feasible, as both were aware of the allocation due to their active involvement in the intervention. Nonetheless, all assessments were conducted by assessors who remained blinded to treatment allocation.

Intervention and Control Groups

During the clinical visits at baseline, 3 months, and 6 months, all patients were educated about the health benefits of regular PA and encouraged to integrate walking into their daily routine.

Patients in the intervention group participated in a 6-month behavioral lifestyle intervention aimed at seamlessly integrating additional PA, primarily walking, into their daily routines. This intervention utilized behavior change techniques, including self-monitoring, goal-setting, and action planning, facilitated by one of two research nurses through regular phone consultations.

At the baseline visit, patients were equipped with a wrist-worn Garmin vívofit activity tracker to self-monitor their daily step count. The Garmin vívofit was chosen for its simplicity, functioning primarily as a pedometer, making it suitable for our study population of older heart failure patients, many of whom had limited experience with advanced smart devices. To maintain this simplicity, we configured the Garmin device to avoid any prompts or feedback. However, we did not prohibit participants from altering the Garmin settings or using the Garmin app, allowing them the discretion to personalize their device experience. This approach mirrors how older individuals might use such devices in real-world settings outside of a controlled study environment. Furthermore, the Garmin vívofit's extended battery life of at least eight months alleviated the burden of frequent charging for patients. Lastly, the Garmin vívofit's step-counting accuracy has been previously validated in both lab-based and free-living environments. Among the devices tested, it emerged as the top-

performing tracker for heart failure patients.[32] Nevertheless, the inherent simplicity of the device meant it lacked features like a heart rate monitor or wear sensor, which posed challenges in verifying consistent wear.

The patients were advised to wear the Garmin device from waking to sleeping. Importantly, participants were instructed not to intentionally increase their activity levels during the initial week to ensure an accurate capture of their habitual daily step count. Furthermore, to bolster patients' adherence to self-monitoring, they were instructed to record their daily steps as indicated by the Garmin device in a paper diary and to review this diary at least once a week.

Approximately two weeks after the baseline visit, patients in the intervention group were contacted by phone by one of the two nurse counselors. The nurse reviewed the patients' average daily step count as recorded by the tracker during the initial week. The patients were then guided to aim for an incremental increase of at least 3,000 steps above their baseline gradually over six weeks. Targeting an additional 3,000 steps daily is a common goal in behavioral interventions.[33] This increment equates to approximately 30 minutes of walking, assuming a pace of 100 steps per minute—a heuristic estimate for a moderate-intensity threshold.[33] As a result, this represents more than 150 minutes of moderate-intensity PA each week, in line with the WHO's guidelines for adults with chronic conditions.[34] Regular engagement at this activity level has consistently been associated with notable health advantages.[34] If patients found the 3,000-step increase challenging, they were encouraged to propose a more achievable goal. Studies have shown that 'goal ownership,' or a deep personal commitment to a set target, often has a stronger influence on behavior change than the exact numerical value of the goal.[35] Therefore, the counselor ensured that patients felt a sense of ownership over their goals rather than feeling they were externally imposed. Additionally, patients were prompted to identify opportunities to incorporate these additional

steps into their daily routines and to formulate their own action plans. Should they encounter challenges in creating these plans, the counselor offered suggestions, such as incorporating walking into daily commutes, post-meal or evening strolls, walking with grandchildren, dog walking, or walking meetings.

In the follow-up phone counseling sessions at 1, 2, 4, and 5 months, the counselor assisted patients in revisiting their step goals and action plans. These sessions focused on addressing any barriers faced, emphasizing the importance of social support, and offering tailored feedback on progress. The counselor also discussed the patients' personal goals, monitored adherence, reviewed their step diaries, and provided guidance on overcoming challenges to PA. Based on the patient's progress, the counselor had the flexibility to adjust the step goals. For example, if a patient regularly surpassed their goal, a higher target might be set. On the other hand, if a patient found the goal unachievable, it could be adjusted downward to maintain motivation and avoid discouragement.

Patients in the control group received usual care, which included education about the health benefits of PA and encouragement to augment their walking routine during clinical visits. However, they did not receive the activity tracker, specific step goals, or regular phone consultations from the research nurse.

Outcomes

The primary outcome was the difference between groups in the distance (in meters) walked during the 6MWT at 6 months.

Secondary outcomes at 6 months encompassed: (a) PA measures: average daily step count and minutes of moderate-to-vigorous PA (MVPA); (b) biomarkers: N-terminal pro–B-type natriuretic peptide (NT-proBNP) and high-sensitivity C-reactive protein (hsCRP); (c) left ventricular ejection fraction; (d) patient-reported outcomes: Beck Depression Inventory-II (BDI-II), 36-item Short-Form Health Survey (SF-36), and General Self-Efficacy Scale

(GSE); (e) anthropometric measures: body mass index, waist and hip circumference; (f) Meta-Analysis Global Group in Chronic Heart Failure (MAGGIC) risk score. The 6MWT, NT-proBNP, and body weight were additionally evaluated at 3 months.

For both the intervention and control groups, PA was objectively measured using the Actigraph wGT3X-BT accelerometer. Participants were instructed to wear the device on their right hip during waking hours for a consecutive 7-day period at baseline and 6 months, ensuring consistent measurement across both groups.[36] This device recorded raw accelerometry data which were then aggregated into 60-second epochs. Non-wear time was identified using Choi's algorithm,[37] and a valid day was defined as having a minimum of 600 minutes of wear time. Only measurements with at least four valid days, including at least one weekend day, were considered for analysis.[38] The average daily step count was determined using the manufacturer's proprietary algorithm as implemented in the ActiLife software, and minutes of moderate-to-vigorous PA (MVPA) were calculated based on Freedson's cut-points.[39] It's important to note that while the intervention group also wore the Garmin activity tracker, the reported values of step count and minutes of MVPA for both groups were obtained solely through the Actigraph accelerometer.

Adherence to the intervention was gauged based on the percentage of subjects who either (a) declined to wear the wrist-worn activity tracker, (b) missed the clinic visit at 3 and 6 months, or (c) participated in fewer than 3 out of the 5 planned phone counseling sessions. Additionally, during each phone contact, we assessed adherence to self-monitoring with the activity tracker by asking patients if they maintained their paper diary and inquiring about their recent step count.

Adverse events were consistently monitored and documented throughout the trial duration. Data concerning hospitalizations, heart failure decompensation, cardiovascular events, falls and injuries, musculoskeletal issues, and fatalities were gathered at each time

point.

Detailed descriptions of all outcomes, including exploratory, can be found in the published protocol and SAP.[27,28]

Statistical Methods

The primary analyses were conducted by the strict intention-to-treat principle utilizing a linear mixed-effect model, accounting for clustering at the center level as a random effect and adjusting for baseline value of the respective variables, age, sex, and NYHA class as fixed effects. Additionally, supplementary analyses were conducted on the per-protocol population using the same approach; the definition of the per-protocol population is detailed in the published SAP.[28] Furthermore, for the primary outcome, a supplementary analysis was undertaken in which missing data were imputed using multiple imputations by chained equations (MICE) with the predictive mean matching method.

Pre-specified subgroup analysis was conducted to assess the differential effect of the intervention on patients participating before (prior to March 11, 2020) versus after the onset of the COVID-19 pandemic. Additional post-hoc subgroup analyses investigated patient subgroups according to baseline 6MWT, daily step count, age, sex, NYHA class, body mass index, NT-proBNP, and MAGGIC risk score. Whether intervention effects were significantly different between the complementary subgroups was assessed by conducting interaction tests, with interaction terms incorporated into the linear mixed-effect models, adjusted for covariates as in the primary analysis.

The intervention effect for the primary outcome is presented as the mean, accompanied by a two-sided 95% confidence interval (95% CI) and the associated p-value (determined at a two-sided 5% significance level). For secondary outcomes, only the mean and 95% CI are reported, as adjustments for multiple testing were not made. For the within-group changes, both means (and 95% CI) and medians (and IQR) are reported, given that the variables did

not exhibit a normal distribution. The normality of the variables was assessed using the Shapiro-Wilk test.

All analyses were conducted using the R statistical software (version 4.1.2) and the packages nlme (3.1-153) and mice (3.15.0).

Results

Study Participants

Out of the 218 patients screened, 11 were excluded and 5 refused to participate (Figure 1). A total of 202 patients were randomized, with a median age of 65 years; 22.8% were women, 90.6% classified as NYHA class II (Table 1). Complete primary outcome data were available for 186 patients, representing 92.1% (Table S1). A CONSORT flowchart detailing the trial's progression is provided in Figure 1. Major and minor protocol violations are detailed in Table S2.

Adherence to Intervention

Of the 101 patients allocated to the intervention group, 19 did not adhere to the pre-specified criteria. Specifically, 3 patients declined to wear the Garmin activity tracker immediately post-randomization, another 3 later during the intervention period, 7 missed their clinic visits at either three or six months, and 14 participated in fewer than three of the five planned counseling sessions. As a result, 82 patients (81%) fully adhered to the intervention.

Of the 84 patients in the intervention group who participated in at least three of the five planned counseling sessions and did not decline to wear the tracker, 70 (83%) consistently kept their diaries, and 77 (92%) consistently provided estimates of their recent step counts during all phone contacts.

Primary Outcome

In the intention-to-treat analysis of the complete cases, the intervention effect on the 6MWT

at 6 months was +7.4 m (95% CI -8.0 to 22.7; p = 0.345). The supplementary analysis following the imputation of missing cases and the per-protocol analysis yielded similar results (Table 2).

Secondary Outcomes

In the intention-to-treat analysis of secondary outcomes at 6 months (Table 3), notable findings include the positive intervention effect on average daily step count (+1420; 95% CI 749 to 2,091) and minutes of MVPA (+8.2; 95% CI 3.0 to 13.3). Results for the intention-to-treat analysis at 3 months are in Table S3. Per-protocol analyses at 6 months (Table S4) and 3 months (Table S5) produced similar results as those conducted by intention-to-treat.

Subgroup Analyses

In the exploratory subgroup analyses of the primary outcome, no significant differences between the subgroups were observed (Figure 2), although there was a numerical improvement in younger, non-obese patients with better functional status and milder disease severity.

Adverse Events

Adverse events for each trial group are detailed in Table 4, where the number of occurrences for each event is presented separately for each trial group. The most frequently recorded adverse events were cardiovascular events including hospitalization for cardiovascular reasons (13 patients). Five patients either visited the emergency room or were hospitalized due to heart failure decompensation and four patients required an increased diuretic dose. Importantly, no adverse events directly related to the intervention were reported.

Discussion

In this randomized controlled trial of a 6-month walking intervention in stable HFrEF patients, no significant improvement in the primary outcome of 6MWT distance was

observed. Among the secondary outcomes, both objective PA measures (step count and time in MVPA) showed significant improvements, as did self-reported general health score; but there were no significant differences in levels of NT-proBNP and hsCRP, ejection fraction, anthropometric measures, depression scores, self-efficacy, most domains of quality of life, and survival risk scores.

The observed improvement in PA by 1420 steps/day—representing an approximately 25% increase—is substantial and equivalent to cardiac rehabilitation studies in cardiovascular patients.[20] It also aligns with findings from other trials evaluating various PA interventions across a range of populations and settings, including patients with chronic conditions[23] as well as healthy[21] and older[22] adults in community settings. In cohort studies with long-term follow-up, the difference of just 1000 steps per day has been associated with a significant decrease in all-cause mortality by 15% in both general population[40] and heart failure patients.[41] Furthermore, the minimum clinically important difference for the physically inactive general population[42] as well as patients with chronic conditions such as chronic obstructive pulmonary disease[43] or peripheral artery disease[44] has been estimated to lie between 500 and 1100 steps per day. Thus, it is noteworthy that while successfully enhancing PA levels, our intervention did not yield a corresponding improvement in functional capacity assessed by the 6MWT.

A plausible explanation for this disconnect could be as simple as the fact that despite a substantial increase in the volume of PA as indicated by step count, the pattern, duration, and intensity of PA were insufficient to elicit changes in the 6MWT.[30,45] Indeed, most cardiac rehabilitation studies showing improvement in 6MWT for HFrEF patients utilized supervised, structured exercises with rigorously prescribed duration and intensity.[8,31] In contrast, our lifestyle walking intervention was more natural, solely focused on increasing the daily number of steps; it was intentionally neither supervised nor structured, and importantly,

did not require specific duration and intensity of PA. As a result, patients in our study could accumulate additional steps in very short bouts and at low intensities, differing from the approach of exercised-based rehabilitation programs, which typically prescribe walking or other exercise modalities in bouts of at least 20 minutes at an intensity above 60% of heart rate reserve.[8,26,46–48] Notably, our study observed an increase of 8 minutes of MVPA per day—equivalent to approximately 800 steps—indicating that the intervention group actually did achieve some of their additional PA at higher intensities. However, the use of minutes of MVPA as a cut-point-based measure has inherent limitations,[49] leaving it uncertain whether the patients reached the intensities typically prescribed in exercised-based cardiac rehabilitation programs.[26,30,48]

An alternative explanation might be that the baseline 6MWT distance of 385 m was near the patients' maximum potential for improvement, suggesting a possible ceiling effect.[50] However, this hypothesis is not supported by our exploratory analysis, which compared subgroups of patients below and above the median baseline 6MWT. Interestingly, patients above the median exhibited greater improvements in 6MWT. This underscores the importance of initial functional capacity in interpreting the potential benefits of interventions on 6MWT outcomes. Another conceivable explanation could be the relatively high initial PA levels of the participants. The benefits of an increased step count are most pronounced in individuals who are the least active, typically averaging around 3000 steps per day.[51] In contrast, our participants had a baseline of approximately 5000 steps, representative of the step count observed in heart failure patients in other studies.[52] Nonetheless, this explanation seems less plausible, as our subgroup analysis revealed that patients with step counts above the median tended to benefit more from the intervention compared to those below the median. Yet another explanation could be the COVID-19 pandemic, which significantly impacted patients' activity levels and could have confounded the results.[53] Exploratory

subgroup analysis indicated that patients who participated before the onset of the pandemic experienced greater (albeit insignificantly) gains in 6MWT than those who participated after the onset. Nonetheless, the improvement of 19 m in the former group was still considerably below the minimal clinically important difference. Therefore, while the COVID-19 pandemic may have had some influence, it is unlikely to fully explain the observed lack of significant improvement in 6MWT in our study.

Results in Context of Other Literature

A limited number of studies have investigated the impact of interventions aiming to enhance the PA of heart failure patients in everyday life outside of structured exercise-based programs, with the majority showing limited success.[6,13] For instance, the REACH-HF trial, which incorporated a progressive walking program, did not elevate overall PA levels nor showed any between-group difference in the incremental shuttle walk test, although it did improve disease-specific health-related quality of life, its primary outcome.[54] The HF-Wii trial adopted a different approach, utilizing home-based exergaming to encourage increased PA in heart failure patients. The intensity of the exergames varied from 2.0 to 4.2 METs, but most participants opted for the lower-intensity games. After adjusting for baseline 6MWT, the trial found no significant differences in the 6MWT, leading the authors to conclude that the intervention might not have been sufficiently intense,[55] rather similar to our results.

In contrast to the aforementioned lifestyle PA interventions, the results from structured exercise-based programs have demonstrated significant improvements in both the 6MWT[30,56] and quality of life.[57,58] Nevertheless, even in these trials, the improvements observed in the 6MWT are often modest and tend to be short-term. For example, the individual participant meta-analysis ExTraMATCH II reported improvements in the 6MWT at 12-month follow-up of 21 meters.[59] Moreover, HF-ACTION, the largest trial of exercise-based rehabilitation to date, identified a significant intervention effect of 15 meters at 3 months, but this effect

disappeared at 12 months.[8] Furthermore, a recent large 9-week telerehabilitation trial, TELEREH-HF, found a significant difference in the 6MWT of only 9 meters.[31] Our trial was not powered to detect such small differences in the 6MWT, and it is debatable whether these differences are clinically relevant.[29]

Strengths and Limitations

Our study has several important strengths. Firstly, our recruitment strategy drew from a range of centers across the Czech Republic, enhancing generalizability. Secondly, our participants' average baseline step count was representative of heart failure patients as observed in other studies,[43] further bolstering external validity. Thirdly, we employed objective assessment methods for PA, utilizing accelerometers, which minimized subjective bias and provided accurate and reliable data on participants' activity levels. Lastly, our study exhibited minimal losses to follow-up, with only an 8% dropout rate, thereby reducing the risk of attrition bias and ensuring a comprehensive analysis of the collected data. These strengths collectively contribute to the robustness and real-world applicability of our study findings.

Several limitations warrant consideration and may influence the interpretation of the findings. Firstly, our study was designed to detect a clinically meaningful change of 45 m in the 6MWT. However, smaller changes that might still be of clinical significance could have been missed. Furthermore, the observed between-group difference of 1,420 steps might not have been substantial enough to elicit a 45-meter improvement in the 6MWT. Consequently, a study powered to detect smaller 6MWT differences, while also achieving more pronounced step count increases, might discern a significant effect on the 6MWT. Besides, the study might not have been powered to detect differences in secondary outcomes. Secondly, the follow-up period of 6 months might not be sufficient to observe the long-term effects of the intervention on functional capacity and other outcomes. The ongoing 12-month follow-up will provide more insights into the long-term sustainability of the observed changes in PA.

Thirdly, due to practical reasons, we could not record the number and characteristics of all patients who were considered for inclusion but did not enter the formal screening using the baseline 6MWT. Fourthly, our study population included a notable proportion of patients with NYHA functional class II and higher baseline 6MWT, which might not be entirely reflective of the broader HFrEF population in more recent clinical trials. This could potentially limit the generalizability of our findings to populations with more pronounced functional limitations. Fifthly, due to the constraints of the study design and to ensure a manageable assessment burden on participants, the study did not include heart failure-specific patient-reported outcomes such as the Kansas City Cardiomyopathy Questionnaire (KCCQ) or the Minnesota Living with Heart Failure Questionnaire (MLWHF), which might have offered a more nuanced assessment of the patients' quality of life in the context of heart failure. Finally, the absence of patient blinding constitutes a significant limitation. Being aware of their group assignment could potentially influence participants' behavior, especially during assessments, thereby introducing bias into the reported outcomes.

Conclusions

Integrating a simple lifestyle walking intervention into the daily life of stable HFrEF patients did not improve their functional capacity, despite having increased their objectively measured PA levels. Achieving improvements in functional capacity likely necessitates the implementation of traditional supervised, structured exercise-based rehabilitation programs with specified durations and intensities. As these programs often fail to induce sustained behavioral change in the long term, future studies should explore the potential of a comprehensive approach that combines exercise-based rehabilitation with simple lifestyle PA interventions, utilizing tools such as activity trackers and mobile apps, to support long-term behavioral change and enhance health outcomes for HFrEF patients.

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Disclosures

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Supplemental Materials

e-Appendices 1 to 4

Tables S1 to S5

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Table 1. Baseline Characteristics.

Characteristic	All Patients (n = 202)	Intervention Group (n = 101)	Control Group (n = 101)
Age at time of randomization, years, median (IQR)	65.0 (56.0–72.8)	65.0 (56.0–72.0)	65.0 (56.0–73.0)
Sex, n (%)			
Male	156 (77.2%)	78 (77.2%)	78 (77.2%)
Female	46 (22.8%)	23 (22.8%)	23 (22.8%)
Marital status, n (%)			
Married	131 (65.5%)	69 (69.7%)	62 (61.4%)
Divorced	24 (12.0%)	10 (10.1%)	14 (13.9%)
Single	20 (10.0%)	10 (10.1%)	10 (9.9%)
Widowed	17 (8.5%)	8 (8.1%)	9 (8.9%)
Living with a partner	8 (4.0%)	2 (2.0%)	6 (5.9%)
Education level, n (%)			
Elementary	16 (8.0%)	7 (7.1%)	9 (8.9%)
Secondary	153 (76.9%)	73 (74.5%)	80 (79.2%)
University	30 (15.1%)	18 (18.4%)	12 (11.9%)
Employment status, n (%)			
Employed	52 (25.9%)	31 (31.0%)	21 (20.8%)
Unemployed	11 (5.5%)	4 (4.0%)	7 (6.9%)
On old age pension	109 (54.2%)	55 (55.0%)	54 (53.5%)
On disability pension	29 (14.4%)	10 (10.0%)	19 (18.8%)
Smoking status, n (%)			
Never smoked	63 (31.2%)	31 (30.7%)	32 (31.7%)
Ex-smoker	105 (52.0%)	55 (54.5%)	50 (49.5%)
Current smoker	34 (16.8%)	15 (14.9%)	19 (18.8%)
Alcohol intake, n (%)			
Does not consume	65 (32.2%)	33 (32.7%)	32 (31.7%)
Occasionally	112 (55.4%)	55 (54.5%)	57 (56.4%)
Regularly consumes	25 (12.4%)	13 (12.9%)	12 (11.9%)
Average daily step count, median (IQR)	5,071 (3,148–7,357)	4,851 (3,049–7,357)	5,343 (3,168–7,265)
Average daily minutes of MVPA, median (IQR)	10.9 (3.2–27.3)	11.1 (3.6–27.3)	10.2 (2.6–27.7)
Distance walked during the 6MWT, m, median (IQR)	385.0 (329.0–425.0)	390.0 (325.0–430.0)	371.0 (329.8–420.0)
Systolic blood pressure, mmHg, median (IQR)	120.0 (109.0–130.0)	120.0 (109.0–130.0)	120.0 (110.0–131.0)
Diastolic blood pressure, mmHg, median (IQR)	77.0 (70.0–80.0)	78.0 (69.0–80.0)	77.0 (70.0–80.0)
Body mass index, kg/m^2, median (IQR)	29.0 (25.8–33.4)	29.7 (26.0–33.6)	28.5 (25.1–33.0)
Waist circumference, cm, median (IQR)	107.0 (97.0–118.0)	109.0 (99.0–118.0)	104.0 (96.8–117.2)

NYHA class, n (%)			
II	183 (90.6%)	92 (91.1%)	91 (90.1%)
III	19 (9.4%)	9 (8.9%)	10 (9.9%)
Left ventricular ejection fraction, %, median (IQR)	32.5 (25.0–36.8)	34.0 (26.0–37.0)	32.0 (25.0–36.0)
NT-proBNP, ng/L, median (IQR)	597.0 (287.0–1,483.0)	597.0 (276.0–1,483.0)	613.5 (293.5–1,480.0)
hsCRP, mg/L, median (IQR)	2.1 (1.0–5.3)	1.9 (1.0–4.8)	2.3 (1.1–5.4)
Creatinine, µmol/L, median (IQR)	93.0 (79.2–113.8)	93.0 (79.5–115.5)	93.0 (79.5–110.5)
eGFR <60 mL/min/1.73 m², n (%)	78 (38.6%)	42 (41.6%)	36 (35.6%)
Ischemic heart disease, n (%)			
Yes	121 (59.9%)	67 (66.3%)	54 (53.5%)
No	81 (40.1%)	34 (33.7%)	47 (46.5%)
MAGGIC score, mean (SD)	19.0 (5.7)	18.6 (5.7)	19.5 (5.7)
Comorbidities, n (%)			
Arterial hypertension	128 (63.4%)	65 (64.4%)	63 (62.4%)
Prior myocardial infarction	96 (47.5%)	51 (50.5%)	45 (44.6%)
History of atrial fibrillation/flutter	63 (31.2%)	33 (32.7%)	30 (29.7%)
Atrial fibrillation/flutter at screening	23 (11.4%)	13 (12.9%)	10 (9.9%)
Peripheral artery disease	21 (10.4%)	9 (8.9%)	12 (11.9%)
History of cardiac arrest	19 (9.4%)	9 (8.9%)	10 (9.9%)
Stroke	15 (7.4%)	8 (7.9%)	7 (6.9%)
Valve procedure	13 (6.4%)	4 (4%)	9 (8.9%)
Type 2 diabetes	78 (38.6%)	37 (36.6%)	41 (40.6%)
COPD	21 (10.4%)	13 (12.9%)	8 (7.9%)
Depression	16 (7.9%)	10 (9.9%)	6 (5.9%)
Bronchial asthma	12 (5.9%)	4 (4%)	8 (7.9%)
History of malignancy	11 (5.4%)	6 (5.9%)	5 (5%)
Device therapy, n (%)			
ICD or CRT-D	114 (56.4%)	57 (56.4%)	57 (56.4%)
CRT-P or CRT-D	52 (25.7%)	31 (30.7%)	21 (20.8%)
Medication, n (%)			
ß blocker	195 (96.5%)	99 (98%)	96 (95%)
ARNI	114 (56.4%)	58 (57.4%)	56 (55.4%)
ACEi	63 (31.2%)	32 (31.7%)	31 (30.7%)
ARB	16 (7.9%)	8 (7.9%)	8 (7.9%)
MRA	159 (78.7%)	78 (77.2%)	81 (80.2%)
SGLT2i	37 (18.3%)	17 (16.8%)	20 (19.8%)
Loop diuretics	160 (79.2%)	77 (76.2%)	83 (82.2%)
Digoxin	27 (13.4%)	13 (12.9%)	14 (13.9%)
Ivabradine	18 (8.9%)	7 (6.9%)	11 (10.9%)

IQR indicates interquartile range; MVPA, moderate-to-vigorous physical activity; 6MWT, six-minute walk test; eGFR, estimated glomerular filtration rate; COPD, chronic obstructive pulmonary disease; ICD, implantable cardioverter-defibrillator; CRT-D, cardiac resynchronization therapy-defibrillator; CRT-P, cardiac resynchronization therapy-pacemaker; ARNI, angiotensin receptor neprilysin inhibitor; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; MRA, mineralocorticoid receptor antagonist; and SGLT2i, sodium-glucose cotransporter 2 inhibitor.

Table 2. Analyses of the Primary Outcome (6-Minute Walk Test) at 6 Months.

	Intervention group				Control group					
Analysis (number of patients included in the analysis)	**Value at baseline, median (IQR)**	**Value at six months, median (IQR)**	**Change, median (IQR)**	**Change, mean (95% CI)**	**Value at baseline, median (IQR)**	**Value at six months, median (IQR)**	**Change, median (IQR)**	**Change, mean (95% CI)**	**Adjusted between-group difference (95% CI)**	**P-value**
Intention-to-treat analysis of the complete cases (n = 186)	388.0 (324.2; 427.0)	417.5 (375.5; 475.5)	40.0 (0.0; 70.0)	35.5 (22.7; 48.3)	373.5 (331.0; 420.0)	400.0 (357.0; 450.0)	34.5 (0.0; 53.8)	28.8 (18.6; 39.0)	7.4 (-8.0; 22.7)	0.345
Intention-to-treat analysis following the imputation of missing cases (n = 202)	390.0 (325.0; 430.0)	420.0 (358.0; 474.0)	38.0 (5.0; 70.0)	35.2 (23.5; 47.0)	372.0 (330.0; 420.0)	400.0 (350.0; 450.0)	31.0 (-4.4; 53.0)	26.9 (17.2; 36.5)	8.7 (-5.6; 22.9)	0.231
Per-protocol analysis (n = 137)	394.0 (330.0; 430.0)	420.0 (374.0; 477.0)	40.0 (2.5; 70.0)	37.1 (21.3; 52.9)	382.5 (331.0; 420.0)	401.5 (365.0; 453.8)	36.0 (-0.0; 58.5)	30.1 (18.9; 41.2)	5.7 (-12.6; 24.0)	0.539

Change in the 6-minute walk test was not normally distributed.

Table 3. Intention-to-treat Analysis of the Secondary Outcomes at 6 Months.

Outcome (number of patients with complete data)	Change in intervention group, median (IQR)	Change in intervention group, mean (95% CI)	Change in control group, median (IQR)	Change in control group, mean (95% CI)	Adjusted between-group difference (95% CI)
Average daily step count (n = 131)	631.4 (-617.1; 1,639.2)	790 (332; 1,247)	-488.0 (-1,899.3; 728.7)	-667 (-1,183; -152)	1420 (749; 2,091)
Average daily minutes of MVPA (n = 131)	0.4 (-3.3; 9.5)	4.9 (1.0; 8.7)	-0.5 (-7.1; 1.5)	-3.1 (-6.8; 0.6)	8.2 (3.0; 13.3)
NT-proBNP, ng/L (n = 190)	-23.0 (-260.0; 162.0)	114 (-370; 598)	-35.0 (-321.0; 155.0)	-220 (-516; 75)	349 (-193; 892)
hsCRP, mg/L (n = 126)	0.0 (-0.6; 0.8)	1.7 (-0.9; 4.2)	-0.1 (-1.5; 0.5)	-0.3 (-2.2; 1.7)	2.1 (-1.0; 5.1)
LVEF, % (n=189)	2.0 (0.0; 6.0)	3.9 (2.5; 5.4)	3.0 (-0.3; 9.0)	3.7 (2.4; 5.0)	0.3 (-1.5; 2.2)
BDI-II (n=177)	-1.0 (-3.0; 1.0)	-0.7 (-1.6; 0.1)	0.0 (-2.0; 1.0)	0.1 (-0.8; 1.0)	-0.8 (-1.9; 0.4)
SF-36: Physical functioning (n=177)	0.0 (-5.0; 10.0)	1.3 (-1.3; 4.0)	0.0 (-5.0; 10.0)	0.2 (-2.9; 3.3)	1.3 (-2.5; 5.2)
SF-36: Role-Physical (n=177)	0.0 (0.0; 25.0)	3.5 (-4.0; 10.9)	0.0 (-25.0; 0.0)	-4.7 (-12.4; 3.0)	8.3 (-1.3; 17.8)
SF-36: Bodily pain (n=177)	0.0 (-20.0; 12.5)	-4.1 (-10.0; 1.8)	0.0 (-10.0; 10.0)	0.3 (-3.4; 4.0)	-4.9 (-11.0; 1.2)
SF-36: General health (n=177)	5.0 (-3.8; 15.0)	6.3 (3.2; 9.4)	0.0 (-5.0; 10.0)	1.3 (-2.0; 4.5)	4.5 (0.7; 8.4)
SF-36: Vitality (n=177)	0.0 (-5.0; 10.0)	2.6 (-0.2; 5.3)	0.0 (-10.0; 10.0)	-0.5 (-3.3; 2.2)	2.4 (-1.3; 6.0)
SF-36: Social functioning (n=177)	0.0 (-12.5; 12.5)	-1.2 (-5.6; 3.3)	0.0 (-12.5; 12.5)	-1.8 (-5.7; 2.1)	0.5 (-4.9; 5.9)
SF-36: Role-Emotional (n=177)	0.0 (0.0; 33.3)	8.9 (0.7; 17.1)	0.0 (0.0; 0.0)	0.7 (-7.3; 8.8)	4.3 (-5.0; 13.7)
SF-36: Mental health (n=177)	0.0 (-8.0; 4.0)	-1.2 (-4.2; 1.8)	0.0 (-8.0; 4.0)	-1.6 (-3.9; 0.6)	0.8 (-2.7; 4.3)
GSE (n=177)	0.0 (-2.5; 3.5)	0.2 (-1.0; 1.3)	0.0 (-2.0; 2.0)	-0.2 (-1.7; 1.3)	0.5 (-1.1; 2.1)
Weight, kg (n=193)	0.0 (-2.0; 2.0)	0.1 (-0.7; 1.0)	1.0 (-0.8; 3.0)	1.1 (0.3; 1.9)	-1.0 (-2.1; 0.1)
Waist circumference, cm (n=190)	0.0 (-2.0; 2.0)	-0.3 (-1.2; 0.5)	0.0 (-1.0; 3.0)	1.8 (-0.5; 4.2)	-1.5 (-3.7; 0.8)
Hip circumference, cm (n=190)	0.0 (-2.0; 2.0)	0.0 (-1.3; 1.2)	0.0 (-1.0; 3.0)	1.9 (-0.4; 4.1)	-0.9 (-3.1; 1.3)
MAGGIC risk score (n = 189)	-1.0 (-2.0; 1.0)	-0.5 (-1.1; 0.0)	-1.0 (-3.0; 0.0)	-1.1 (-1.7; -0.5)	0.4 (-0.4; 1.2)

The change in none of the variables followed a normal distribution.
MVPA indicates moderate-to-vigorous physical activity; LVEF, left ventricular ejection fraction; BDI-II, Beck depression inventory-II; SF-36, 36-item short-form health survey; and GSE, General self-efficacy scale.

Table 4. Adverse Events.

Adverse event category	All patients (n = 202)	Intervention group (n = 101)	Control group (n = 101)
Hospitalization for heart failure	4	1	3
Visit to the emergency room for heart failure	1	0	1
Increase in diuretic dose	4	1	3
Other CV events including hospitalizations for CV reasons	13	5	8
Non-CV events including hospitalizations for non-CV reasons	9	8	1
ICD discharge	6	4	2
Fall, injury	2	0	2
Infection	9	5	4
Others	3	2	1
Death	1	1*	0
Total	**52**†	**27**	**25**

CV indicates cardiovascular; and ICD, implantable cardioverter-defibrillator.
*The only death was for non-CV reason.
†In total, 52 adverse events were recorded in 42 patients.

Figure Legends

Figure 1. Study enrollment, randomization, and follow-up

Figure 2. Subgroup analyses of the primary outcome (6-minute walk test) at 6 months