The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 15, 2021 VOL. 385 NO. 3

# Physical Rehabilitation for Older Patients Hospitalized for Heart Failure

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## ABSTRACT

### BACKGROUND

Older patients who are hospitalized for acute decompensated heart failure have high rates of physical frailty, poor quality of life, delayed recovery, and frequent rehospitalizations. Interventions to address physical frailty in this population are not well established.

### METHODS

We conducted a multicenter, randomized, controlled trial to evaluate a transitional, tailored, progressive rehabilitation intervention that included four physical-function domains (strength, balance, mobility, and endurance). The intervention was initiated during, or early after, hospitalization for heart failure and was continued after discharge for 36 outpatient sessions. The primary outcome was the score on the Short Physical Performance Battery (total scores range from 0 to 12, with lower scores indicating more severe physical dysfunction) at 3 months. The secondary outcome was the 6-month rate of rehospitalization for any cause.

### RESULTS

A total of 349 patients underwent randomization; 175 were assigned to the rehabilitation intervention and 174 to usual care (control). At baseline, patients in each group had markedly impaired physical function, and 97% were frail or prefrail; the mean number of coexisting conditions was five in each group. Patient retention in the intervention group was 82%, and adherence to the intervention sessions was 67%. After adjustment for baseline Short Physical Performance Battery score and other baseline characteristics, the least-squares mean (±SE) score on the Short Physical Performance Battery at 3 months was 8.3±0.2 in the intervention group and 6.9±0.2 in the control group (mean between-group difference, 1.5; 95% confidence interval [CI], 0.9 to 2.0; P<0.001). At 6 months, the rates of rehospitalization for any cause were 1.18 in the intervention group and 1.28 in the control group (rate ratio, 0.93; 95% CI, 0.66 to 1.19). There were 21 deaths (15 from cardiovascular causes) in the intervention group and 16 deaths (8 from cardiovascular causes) in the control group. The rates of death from any cause were 0.13 and 0.10, respectively (rate ratio, 1.17; 95% CI, 0.61 to 2.27).

### CONCLUSIONS

In a diverse population of older patients who were hospitalized for acute decompensated heart failure, an early, transitional, tailored, progressive rehabilitation intervention that included multiple physical-function domains resulted in greater improvement in physical function than usual care. (Funded by the National Institutes of Health and others; REHAB-HF ClinicalTrials.gov number, NCT02196038.)

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A list of the investigators in this trial is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on May 16, 2021, at NEJM.org.

N Engl J Med 2021;385:203-16.
DOI: 10.1056/NEJMoa2026141

A Quick Take is available at NEJM.org

Acute decompensated heart failure is the leading cause of hospitalization among older persons in the United States[1] and is associated with poor health-related quality of life, frequent rehospitalizations, high mortality, and costs exceeding $39 billion per year.[1,2] Most intervention trials in acute decompensated heart failure have had neutral results, which suggests that outcomes may be driven in part by mechanisms that have been overlooked.[3-5]

Among older patients with acute heart failure, physical function is markedly impaired, and frailty rates and the burden of coexisting conditions are high.[5-8] Even among older patients with stable and well-compensated heart failure, severe impairments in physical function are often present owing to the combined effects of aging, cardiovascular dysfunction, and skeletal-muscle dysfunction.[9,10] As patients with chronic heart failure transition to acute decompensated heart failure, physical function worsens further, and this decline is exacerbated by hospitalization and bed rest.[8] These deficits often persist. Many patients never recover baseline function, lose independence, and have high risks of rehospitalization and death after discharge (sometimes referred to as "post-hospital syndrome").[4,5,11-14]

However, management guidelines do not address physical dysfunction in patients hospitalized for heart failure,[15] and previous exercise training trials excluded patients with heart failure who had recently been hospitalized.[10,16] To address these issues, we conducted the Rehabilitation Therapy in Older Acute Heart Failure Patients (REHAB-HF) trial, a multicenter, randomized, single-blind, controlled trial of an early, transitional, tailored, progressive rehabilitation intervention that included multiple physical-function domains. We hypothesized that the intervention would improve physical function and reduce rates of rehospitalization for any cause at 6 months.

## Methods

### Trial Design and Oversight

Details of the trial design and intervention methods have been described previously.[17,18] The organizational structure is shown in Figure S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org. The steering committee designed the trial and oversaw operations. The protocol, which is available at NEJM.org, was approved by the institutional review board at each site. An independent data and safety monitoring committee evaluated patient safety. The authors vouch for the accuracy and completeness of the data and analyses and for the fidelity of the trial to the protocol.

### Patients and Randomization

Patients were screened at the time of hospital admission and were enrolled before discharge. Patients were eligible for participation if they were 60 years of age or older, if they had been admitted for acute decompensated heart failure regardless of ejection fraction, if they could walk at least 4 m at enrollment (with or without the aid of an assistive device), if they were functionally independent before admission, and if they were expected to be discharged home. Full details of the inclusion and exclusion criteria are provided in the Supplementary Appendix.[17] After eligible patients provided written informed consent and completed baseline testing, they were randomly assigned with equal probability to the rehabilitation intervention (intervention group) or to usual care (control group) by a centralized, Web-based system, with the use of block randomization. Randomization was stratified according to ejection fraction (<45% vs. ≥45%) and clinical site. The patients in both trial groups received usual care, as recommended by their medical providers, which could include inpatient or outpatient physical therapy and standard cardiac rehabilitation.

### Trial Procedures

The trial intervention (for the intervention group) was an early, transitional, tailored, progressive physical rehabilitation program that had been developed for frail, older patients with acute decompensated heart failure.[18,19] The intervention focused on four physical-function domains (strength, balance, mobility, and endurance) and progressed through four prespecified functional levels within each domain (Table S1). The progression of exercise intensity and the types of exercises at each session were individualized on the basis of the patient's performance level within each domain.[18] A key goal was to increase each patient's endurance (duration of walking); doing this safely required first addressing deficits in balance, strength, and mobility.

The intervention was initiated in the hospital when feasible and was subsequently transitioned to an outpatient facility as soon as possible after discharge. If needed, home-based sessions were provided by interventionists until the patient was physically able to attend the facility-based outpatient sessions. Outpatient sessions were 60 minutes long, occurred 3 days per week for 12 weeks (or 36 sessions), and were conducted at a 1:1 interventionist–patient ratio. Outpatient sessions were complemented by home exercise (low-intensity walking, which was gradually increased to up to 30 minutes daily, and strengthening exercises) on nonprogram days. The home exercise component of the intervention was initiated only after a visit to the patient's home by an interventionist to evaluate the home environment.[18]

A key goal of the intervention during the first 3 months (the outpatient phase) was to prepare the patient to transition to the independent maintenance phase (months 4 through 6). At the 3-month visit, patients were provided with individualized exercise prescriptions and were subsequently followed every 4 weeks by telephone contact. Patient retention in the intervention group and adherence to the intervention sessions were reviewed and discussed every 2 weeks by a dedicated committee in accordance with the recommendations of the National Institutes of Health Behavior Change Consortium Treatment Fidelity Workgroup.[18] Additional details regarding the intervention are provided in the Supplementary Appendix.

Patients who had been randomly assigned to the control group received a telephone call every 2 weeks and had in-person clinic visits at 1 month and 3 months after discharge from the index hospitalization.[17] Information regarding the occurrence of symptoms or clinical events and the receipt of rehabilitation therapy unrelated to the trial was collected. Patients received no specific recommendations with respect to exercise, but they were encouraged to adhere to prescribed usual-care therapy and follow-up appointments. Additional details regarding the control group are provided in the Supplementary Appendix.

### TRIAL OUTCOMES

Outcome measures of physical and cognitive function were assessed by personnel who were unaware of the trial-group assignments. Physical function, quality of life, depression, and cognitive function were assessed at baseline in the hospital and at 3 months.[17] Clinical events were ascertained throughout follow-up from monthly interviews and from review of medical records.

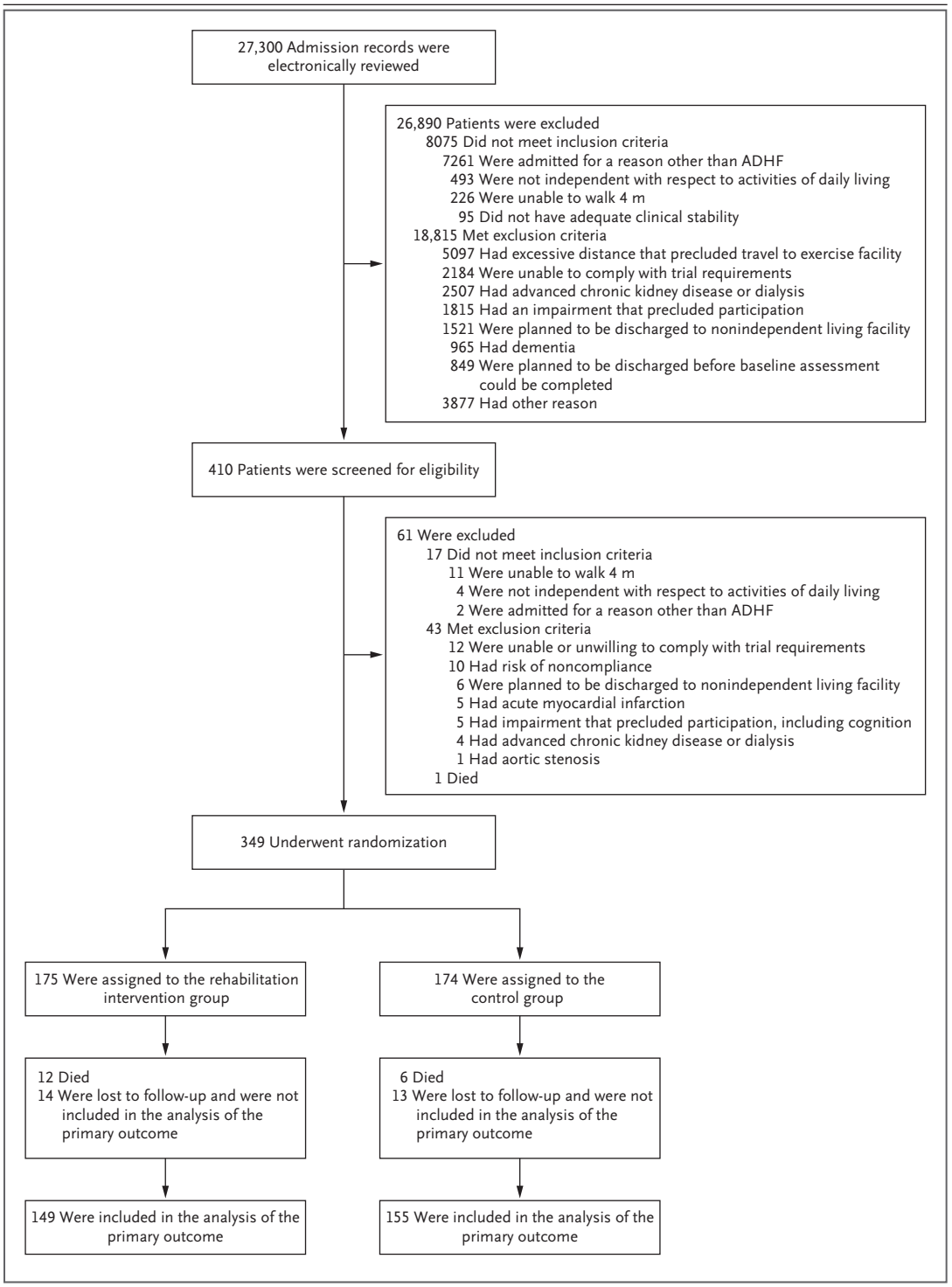
The primary outcome was the score on the Short Physical Performance Battery at 3 months. The Short Physical Performance Battery is a standardized, reproducible measure of global physical function that has been validated in frail, older persons and predicts a wide range of clinical outcomes.[20-22] It has three components: a standing balance test, a gait-speed (4-m walk) test, and a strength test (as assessed by the time needed to rise from a chair five times). Each component is scored on a scale of 0 to 4; the sum of the scores ranges from 0 to 12, with lower scores indicating more severe physical dysfunction.

The secondary outcome was the rate of rehospitalization for any cause at 6 months, with rehospitalization defined as any hospital stay longer than 24 hours. The reasons for rehospitalization were categorized as noncardiovascular cause, heart failure, or another cardiovascular cause by an independent adjudicator who was unaware of the trial-group assignments.

Additional physical-function outcomes included 6-minute walk distance, frailty status (assessed according to modified Fried criteria[6]), hand-grip strength, and gait speed at 3 months. Quality of life was assessed at 3 months with the use of the Kansas City Cardiomyopathy Questionnaire (KCCQ) and the EQ-5D-5L (also known as the European Quality of Life 5-Dimension 5-Level questionnaire) visual-analogue scale. Other outcomes included the Geriatric Depression Scale–15 score and the Montreal Cognitive Assessment score.

### STATISTICAL ANALYSIS

On the basis of the results from a pilot study,[19] we estimated that 258 patients who could be evaluated for efficacy would provide the trial with 80% power to detect a 10% difference (equivalent to a difference of 0.6 points) between the intervention group and the control group in the score on the Short Physical Performance Battery at 3 months (the primary outcome); the enrollment of 334 patients who could be evaluated for efficacy would be needed to detect a 25% difference in the rate of rehospitalization at 6 months (the secondary outcome). We planned to enroll




360 patients in order to allow for approximately 7% of the patients to withdraw from the trial.

Baseline characteristics are presented as means and standard deviations for continuous variables and as counts and percentages for categorical variables. To account for deaths and loss to follow-up, joint models of continuous and survival outcomes were used to assess differences between the intervention group and the control group in the 3-month outcomes (includ-

**Figure 1 (facing page). Screening and Randomization.**
A total of 27,300 hospital admission records were electronically reviewed; these included multiple repeat admissions and thus should not be construed as unique, individual patients. The most common reason for not meeting the inclusion criteria was that heart failure was not the reason for hospital admission (7261 patients). The most common exclusion criterion was an excessive distance that precluded travel to the exercise facility (5097 patients), which was generally defined as a driving time of more than 1 hour each way. Detailed reasons for exclusion are provided in Table S2. A total of 410 patients had full, in-person screening visits, of whom 349 were enrolled. Of these, 304 had available data for the analysis of the primary outcome. Figure S2 shows screening and randomization information for the secondary outcome. ADHF denotes acute decompensated heart failure.

ing the primary outcome), with adjustment for baseline measures.[23] Differences between the two groups in the rate of rehospitalization (for any cause and for heart failure) and in the number of days of rehospitalization were assessed with the use of joint models similar to those described above, with a Poisson distribution for clinical events based on counts and a negative binomial distribution for days of rehospitalization for any cause to account for overdispersion. Differences between the two groups in the rate of death and in the rate of combined rehospitalization for any cause and death were assessed with the use of generalized linear models, with a Poisson distribution. Differences in proportion-based (binary) clinical measures were analyzed with the use of logistic regression. All the models were adjusted for clinical site, ejection fraction category, age, and sex. The secondary outcome was adjusted for the baseline score on the Short Physical Performance Battery. The potential consistency of intervention effects among prespecified subgroups for the primary outcome was examined with the use of forest plots.

For the primary outcome, a two-tailed P value of less than 0.05 was considered to indicate statistical significance. For all other outcomes, effect-size estimates and 95% confidence intervals are reported without P values. The widths of the confidence intervals were not adjusted for multiple comparisons, so the intervals should not be used to infer definitive treatment effects for the secondary outcome or other outcomes. Analyses were performed with SAS Enterprise Guide, version 7.11, and SAS software, version 9.4.

## RESULTS

### TRIAL POPULATION AND BASELINE CHARACTERISTICS

The first patient was enrolled in September 2014, and the last patient was enrolled in September 2019. A total of 27,300 hospital admission records (which included multiple repeat admissions and thus did not represent unique patients) were electronically reviewed. Ultimately, 410 patients were screened for eligibility, and 349 were enrolled; 175 were randomly assigned to the intervention group and 174 to the control group. Data were available for analysis of the primary and secondary outcomes for 87% and 99% of the patients, respectively (Fig. 1 and Fig. S2).

The demographic and clinical characteristics of the patients at baseline are shown in Table 1 and in Table S3. The mean (±SD) age was 72.7±8.1 years, 52% of the patients were women, and 49% were non-White (of whom 94% were Black). The cause of heart failure was ischemic heart disease in 35% of the patients, and 53% had preserved ejection fraction. Patients had high burdens of coexisting conditions, and the incidences of previous hospitalization for any cause and previous hospitalization for heart failure were high (approximately 45% and 25%, respectively). Most (97%) of the patients were assessed as frail or prefrail, according to the modified Fried criteria. Urinary incontinence, falls, and depression were common. The incidence of diabetes mellitus was higher in the intervention group than in the control group (58% vs. 47%). At baseline, the patients were assessed as having severely impaired physical function, poor quality of life, and at least mild cognitive dysfunction (Table 2).

### FOLLOW-UP AND TRIAL OUTCOMES

The last follow-up visit was in March 2020. Among the 175 patients who had been randomly assigned to the rehabilitation intervention, 12 died before completing the intervention, 14 were lost to follow-up for the analysis of the primary outcome, and 16 permanently discontinued the intervention but were included in the analyses of the primary and secondary outcomes. In an analysis that excluded patients who died, patient retention in the intervention group was 82%, and patients completed a mean (±SE) of 24.3±1.0 outpatient intervention sessions; adherence to the sessions was 67±3% (Fig. S3 and Table S4). After adjustment for sessions missed because of med-

ical appointments and illness, adherence to the intervention was 78±3%. Patients generally progressed to higher functional levels in each domain during the course of the intervention (Fig. 2). A key goal was to increase each patient's exercise endurance (duration of walking); among patients who participated in the first and last sessions, the mean (±SD) endurance doubled from 10.7±5.9 minutes in the first session to 22.0±11.1 minutes in the last session. Additional data regarding exercise during the hospitalization, outpatient, and maintenance phases are provided in Tables S5 through S7; information regarding usual-care exercise therapy not associated with the trial is provided in Table S8.

After adjustment for the baseline Short Physical Performance Battery score and other baseline characteristics, the least-squares mean (±SE) score on the Short Physical Performance Battery at 3 months was 8.3±0.2 in the intervention group and 6.9±0.2 in the control group (mean between-group difference, 1.5; 95% confidence interval [CI], 0.9 to 2.0; P<0.001) (Table 2 and Fig. S4). This effect appeared to be relatively uniform across a wide variety of prespecified subgroups (Fig. 3). The results for each of the three components of the Short Physical Performance Battery are shown in Table 2. The benefit of the rehabilitation intervention persisted after post hoc adjustment for baseline imbalances in diagnoses of diabetes and peripheral vascular disease; the least-squares mean score was 8.3±0.2 in the intervention group and 6.8±0.2 in the control group (mean between-group difference, 1.5; 95% CI, 0.9 to 2.1).

The secondary outcome, the rate of rehospitalization for any cause at 6 months, showed no appreciable difference between the intervention group and the control group, with rates of 1.18 and 1.28, respectively (rate ratio, 0.93; 95% CI, 0.66 to 1.19) (Table 2). The exploratory outcomes, including 6-minute walk distance, gait speed, hand-grip strength, frailty status, quality of life, cognition, depression, and clinical events including falls and rehospitalizations, are shown in Table 2 and Figure S5.

There were 21 deaths in the intervention group and 16 deaths in the control group; the rates of death were 0.13 and 0.10, respectively (rate ratio, 1.17; 95% CI, 0.61 to 2.27) (Table 2). Among these deaths, 15 in the intervention group and 8 in the control group were from cardiovascular causes (Table S9). Serious and nonserious adverse events are summarized in Tables S10 and S11. Chest pain, hypertension, dizziness, hyperglycemia, and hypoglycemia were more common in the intervention group than in the control group, and falls and heart failure were more common in the control group.

## DISCUSSION

The REHAB-HF trial examined the effects of an early, transitional, tailored, progressive rehabilitation intervention that included multiple physical-function domains in frail, older patients who were hospitalized for acute decompensated heart failure. The intervention group had significantly greater improvement in physical function, as assessed by the score on the Short Physical Performance Battery at 3 months, than the control group. The results of the analyses of 6-minute walk distance, frailty status, quality of life, and depression also suggested clinical benefits of the intervention. Over the course of 6 months, the incidence of rehospitalization for any cause, rehospitalization for heart failure, and death was high in both groups.

Our trial was designed to address several critical evidence gaps regarding physical rehabilitation in patients with heart failure. Most previous trials excluded patients who had been hospitalized within the previous 6 weeks — a period during which the severity of physical dysfunction and the risk of clinical events are highest; those trials also involved few older, frail patients with multiple coexisting conditions in whom different approaches may be appropriate.[3,10] In previous early trials of rehabilitation after heart failure, enrollment of the patients and initiation of the intervention began, on average, 7 weeks after hospital discharge; traditional endurance exercise training was commonly used[24,25]; the enrolled patients were younger and much less frail and diverse than those in our trial[25]; there was no control group[24,26]; and the trials were unblinded[25,27] and often small, single-center trials.[27] One of the largest of such trials involving recently hospitalized patients, EJECTION-HF (Exercise Joins Education: Combined Therapy to Improve Outcomes in Newly-Discharged Heart Failure), showed no benefit of the intervention over usual care with

**Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.***

| Characteristic | Intervention (N=175) | Control (N=174) |
|---|---|---|
| Age — yr | 73.1±8.5 | 72.2±7.7 |
| Female sex — no. (%) | 85 (49) | 98 (56) |
| Non-White race — no. (%)† | 81 (46) | 91 (52) |
| Body-mass index‡ | 32.9±8.2 | 33.0±8.9 |
| Ejection fraction ≥45%, indicating preserved ejection fraction — no. (%) | 93 (53) | 92 (53) |
| Heart failure caused by ischemic heart disease — no. (%)§ | 66 (38) | 56 (32) |
| NYHA class — no. (%) | | |
| II | 33 (19) | 34 (20) |
| III | 100 (57) | 90 (52) |
| IV | 41 (23) | 51 (29) |
| Median B-type natriuretic peptide (IQR) — pg/ml¶ | 595 (259–1292) | 645 (381–1072) |
| Median N-terminal pro–B-type natriuretic peptide (IQR) — pg/ml‖ | 2527 (1395–4858) | 3615 (1874–8637) |
| Median no. of days hospitalized during index hospitalization (IQR) | 4 (3–7) | 5 (3–7) |
| Patients with ≥1 hospitalization in previous 6 mo — no. (%) | 76 (43) | 80 (46) |
| Coexisting conditions | | |
| Total no. of coexisting conditions | 5.4±2.0 | 5.0±1.9 |
| Hypertension — no. (%) | 159 (91) | 162 (93) |
| History of myocardial infarction — no. (%) | 31 (18) | 32 (18) |
| History of coronary revascularization, including PCI and CABG — no. (%) | 55 (31) | 47 (27) |
| Atrial fibrillation — no. (%) | 89 (51) | 87 (50) |
| Diabetes mellitus — no. (%) | 101 (58) | 81 (47) |
| Hyperlipidemia — no. (%) | 110 (63) | 120 (69) |
| Depression, according to electronic medical record — no. (%) | 29 (17) | 33 (19) |
| Geriatric conditions | | |
| Dementia or cognitive impairment, according to electronic medical record — no. (%) | 6 (3) | 4 (2) |
| Frail, as defined by the presence of at least three Fried criteria** — no. (%) | 92 (53) | 100 (57) |
| Prefrail, as defined by the presence of one or two Fried criteria** — no. (%) | 77 (44) | 68 (39) |
| Urinary incontinence — no./total no. (%) | 19/144 (13) | 21/142 (15) |
| Patients with falls in previous 3 mo — no./total no. (%) | 24/143 (17) | 20/146 (14) |

* Plus–minus values are means ±SD. CABG denotes coronary artery bypass graft, IQR interquartile range, NYHA New York Heart Association, and PCI percutaneous coronary intervention.
† Race was reported by the patient.
‡ The body-mass index is the weight in kilograms divided by the square of the height in meters.
§ Ischemic heart disease was determined to be the cause of heart failure if a patient had a history of myocardial infarction, coronary revascularization, or both.
¶ This analysis included data from 104 patients in the intervention group and 100 patients in the control group.
‖ This analysis included data from 58 patients in the intervention group and 59 patients in the control group.
** The five Fried criteria include weight loss, exhaustion, low physical activity, slow gait speed, and weak hand-grip strength.

**Table 2. Trial Outcomes.**

| Outcome | Intervention (N=175) | Control (N=174) | Effect Size (95% CI) |
|---|---|---|---|
| **Outcomes at 3 mo*** | | | |
| SPPB score, primary outcome† | | | |
| At baseline | 6.0±2.8 | 6.1±2.6 | |
| At 3 mo | 8.3±0.2 | 6.9±0.2 | 1.5 (0.9 to 2.0)‡ |
| No. of patients assessed at 3 mo | 149 | 155 | |
| Balance score | | | |
| At baseline | 2.6±1.3 | 2.7±1.3 | |
| At 3 mo | 3.2±0.1 | 2.9±0.1 | 0.4 (0.1 to 0.6) |
| 4-M walk score | | | |
| At baseline | 2.3±1.0 | 2.3±1.0 | |
| At 3 mo | 3.0±0.1 | 2.5±0.1 | 0.5 (0.2 to 0.7) |
| Chair rise score | | | |
| At baseline | 1.1±1.2 | 1.2±1.2 | |
| At 3 mo | 2.1±0.1 | 1.5±0.1 | 0.6 (0.4 to 0.9) |
| 6-Min walk distance — m | | | |
| At baseline | 194±104 | 193±107 | |
| At 3 mo | 293±8 | 260±8 | 34 (12 to 56) |
| No. of patients assessed at 3 mo | 135 | 125 | |
| Gait speed — m/sec | | | |
| At baseline | 0.60±0.23 | 0.61±0.22 | |
| At 3 mo | 0.80±0.02 | 0.68±0.02 | 0.12 (0.07 to 0.16) |
| No. of patients assessed at 3 mo | 146 | 143 | |
| Hand-grip strength — kg | | | |
| Men | | | |
| At baseline | 30.3±9.5 | 30.5±10.7 | |
| At 3 mo | 30.1±0.7 | 30.6±0.8 | −0.5 (−2.5 to 1.6) |
| No. of patients assessed at 3 mo | 75 | 63 | |
| Women | | | |
| At baseline | 20.7±7.3 | 19.6±6.6 | |
| At 3 mo | 21.3±0.6 | 21.4±0.5 | −0.2 (−1.7 to 1.4) |
| No. of patients assessed at 3 mo | 68 | 76 | |
| Frailty status — no. of modified Fried criteria met§ | | | |
| At baseline | 2.3±1.1 | 2.4±1.1 | |
| At 3 mo | 1.4±0.1 | 1.6±0.1 | −0.3 (−0.5 to 0) |
| No. of patients assessed at 3 mo | 142 | 129 | |
| KCCQ overall score¶ | | | |
| At baseline | 40±21 | 42±21 | |
| At 3 mo | 69±2 | 62±2 | 7.1 (2.0 to 12.2) |
| No. of patients assessed at 3 mo | 147 | 145 | |

**Table 2. (Continued.)**

| Outcome | Intervention (N=175) | Control (N=174) | Effect Size (95% CI) |
|---|---|---|---|
| EQ-5D-5L visual-analogue scale score‖ | | | |
| At baseline | 58±22 | 58±21 | |
| At 3 mo | 71±2 | 65±2 | 7.0 (2.3 to 11.6) |
| No. of patients assessed at 3 mo | 148 | 144 | |
| MoCA score** | | | |
| At baseline | 21.9±4.2 | 21.8±4.5 | |
| At 3 mo | 22.2±0.3 | 22.5±0.3 | –0.2 (–1.0 to 0.6) |
| No. of patients assessed at 3 mo | 144 | 140 | |
| Geriatric Depression Scale–15 score†† | | | |
| At baseline | 4.7±3.3 | 4.7±3.4 | |
| At 3 mo | 3.3±0.2 | 4.1±0.2 | –0.7 (–1.3 to –0.1) |
| No. of patients assessed at 3 mo | 147 | 143 | |
| **Clinical events at 6 mo*** | | | |
| No. of patients | 174 | 173 | |
| Rehospitalization for any cause, secondary outcome — no. of events (rate) | 194 (1.18) | 213 (1.28) | 0.93 (0.66 to 1.19)‡‡ |
| Death — no. of events (rate) | 21 (0.13) | 16 (0.10) | 1.17 (0.61 to 2.27)‡‡ |
| Combined rehospitalization for any cause and death — no. of events (rate) | 215 (1.31) | 229 (1.38) | 0.93 (0.77 to 1.12)‡‡ |
| Rehospitalization for heart failure — no. of events (rate) | 94 (0.57) | 110 (0.66) | 0.89 (0.56 to 1.22)‡‡ |
| No. of patients with ≥2 rehospitalizations for any cause (%) | 47 (27) | 60 (35) | 0.71 (0.44 to 1.13)§§ |
| No. of patients with ≥2 rehospitalizations for heart failure (%) | 22 (13) | 27 (16) | 0.78 (0.41 to 1.46)§§ |
| No. of days of rehospitalization for any cause | 7.2 | 7.6 | 0.92 (0.52 to 1.22)‡‡ |
| No. of patients with ≥1 fall (%) | 48 (28) | 62 (36) | 0.67 (0.42 to 1.06)§§ |
| No. of patients with ≥1 fall that resulted in injury (%) | 12 (7) | 16 (9) | 0.66 (0.30 to 1.47)§§ |

* Baseline data are presented as means ±SD. Follow-up data at 3 months are presented as least-squares means ±SE, with adjustment for baseline value, clinical site, age, sex, and ejection fraction category. The effect sizes for the 3-month outcomes are shown as between-group differences in the least-squares mean change. The widths of the confidence intervals (CIs) have not been adjusted for multiple comparisons, so the intervals should not be used to infer definitive treatment effects for the secondary outcome and other outcomes.

† Total scores on the Short Physical Performance Battery (SPPB) range from 0 to 12, with lower scores indicating more severe physical dysfunction; each component (the standing balance test, the gait-speed test [as assessed by a 4-m walk], and the strength test [as assessed by the time needed to rise from a chair five times]) is scored on a scale of 0 to 4.

‡ P<0.001.

§ For the comparison of the baseline and follow-up results in this trial, the Fried criteria were modified to exclude the weight-loss criterion owing to difficulty in ascertaining weight changes because of changes in fluid status.

¶ Scores on the Kansas City Cardiomyopathy Questionnaire (KCCQ) range from 0 to 100, with higher scores indicating better health status.

‖ Scores on the EQ-5D-5L (also known as the European Quality of Life 5-Dimension 5-Level questionnaire) visual-analogue scale range from 0 to 100, with higher scores indicating better health status.

** Scores on the Montreal Cognitive Assessment (MoCA) range from 0 to 30, with higher scores indicating better cognitive function.

†† Scores on the Geriatric Depression Scale-15 range from 0 to 15, with higher scores indicating worse depressive symptoms.

‡‡ The effect size is shown as a rate ratio.

§§ The effect size is shown as an odds ratio.

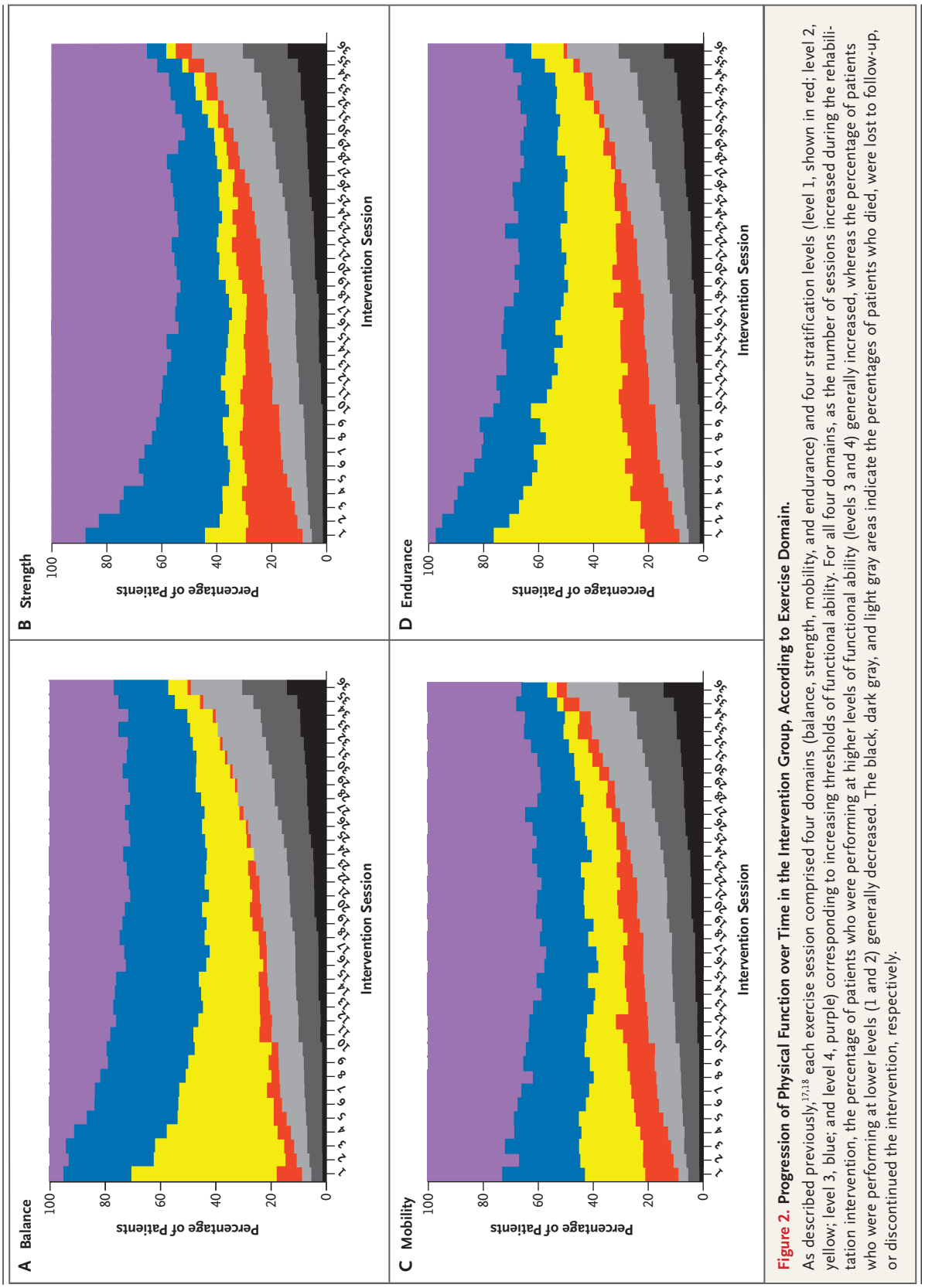



**Figure 2. Progression of Physical Function over Time in the Intervention Group, According to Exercise Domain.**

As described previously,[17,18] each exercise session comprised four domains (balance, strength, mobility, and endurance) and four stratification levels (level 1, shown in red; level 2, yellow; level 3, blue; and level 4, purple) corresponding to increasing thresholds of functional ability. For all four domains, as the number of sessions increased during the rehabilitation intervention, the percentage of patients who were performing at higher levels of functional ability (levels 3 and 4) generally increased, whereas the percentage of patients who were performing at lower levels (1 and 2) generally decreased. The black, dark gray, and light gray areas indicate the percentages of patients who died, were lost to follow-up, or discontinued the intervention, respectively.

| Subgroup | Intervention | Control | Between-Group Difference in Mean Score (95% CI) |
|---|---|---|---|
| | *no. of patients (mean score on SPPB)* | | *points* |
| Overall | 149 (8.3±0.2) | 155 (6.9±0.2) | 1.5 (0.9 to 2.0) |
| Age | | | |
| <70 yr | 63 (7.9±0.3) | 74 (6.7±0.3) | 1.2 (0.4 to 2.1) |
| ≥70 yr | 86 (8.0±0.3) | 81 (6.3±0.3) | 1.6 (0.9 to 2.4) |
| Sex | | | |
| Male | 78 (7.4±0.3) | 69 (6.4±0.3) | 1.0 (0.1 to 1.8) |
| Female | 71 (8.5±0.3) | 86 (6.6±0.3) | 1.9 (1.1 to 2.7) |
| Race | | | |
| Non-White | 67 (7.8±0.3) | 80 (6.6±0.3) | 1.2 (0.4 to 2.1) |
| White | 82 (8.1±0.3) | 75 (6.4±0.3) | 1.7 (0.9 to 2.5) |
| Ejection fraction | | | |
| <45% | 65 (8.1±0.3) | 76 (7.0±0.3) | 1.1 (0.3 to 2.0) |
| ≥45% | 84 (7.8±0.3) | 79 (6.0±0.3) | 1.7 (1.0 to 2.5) |
| NYHA class | | | |
| II | 31 (8.9±0.5) | 28 (5.9±0.5) | 3.0 (1.7 to 4.3) |
| III or IV | 118 (7.7±0.3) | 127 (6.6±0.3) | 1.1 (0.4 to 1.7) |
| Atrial fibrillation | | | |
| No | 72 (8.2±0.3) | 80 (6.7±0.3) | 1.5 (0.6 to 2.3) |
| Yes | 77 (7.7±0.3) | 75 (6.2±0.3) | 1.5 (0.7 to 2.3) |
| Ischemic heart disease | | | |
| No | 95 (8.2±0.3) | 109 (6.7±0.3) | 1.5 (0.8 to 2.2) |
| Yes | 54 (7.5±0.4) | 46 (6.1±0.4) | 1.4 (0.4 to 2.4) |
| Diabetes mellitus | | | |
| No | 63 (8.3±0.3) | 83 (6.8±0.3) | 1.5 (0.7 to 2.3) |
| Yes | 86 (7.8±0.3) | 72 (6.2±0.3) | 1.5 (0.7 to 2.3) |
| Obesity | | | |
| BMI <30 | 59 (7.9±0.4) | 62 (6.8±0.3) | 1.1 (0.2 to 2.0) |
| BMI ≥30 | 90 (8.0±0.3) | 93 (6.3±0.3) | 1.7 (1.0 to 2.4) |
| Overweight or obesity | | | |
| BMI <25 | 24 (8.0±0.5) | 30 (6.3±0.5) | 1.7 (0.3 to 3.1) |
| BMI ≥25 | 125 (8.0±0.3) | 125 (6.6±0.3) | 1.4 (0.8 to 2.0) |
| COPD | | | |
| No | 100 (8.1±0.3) | 119 (6.3±0.3) | 1.8 (1.1 to 2.5) |
| Yes | 49 (7.7±0.4) | 36 (7.1±0.4) | 0.6 (–0.5 to 1.7) |
| Chronic kidney disease | | | |
| No | 100 (8.2±0.3) | 106 (7.0±0.3) | 1.2 (0.5 to 1.9) |
| Yes | 49 (7.6±0.4) | 49 (5.6±0.4) | 2.0 (1.0 to 3.0) |
| Depression | | | |
| No | 125 (8.0±0.3) | 125 (6.4±0.3) | 1.6 (0.9 to 2.2) |
| Yes | 24 (7.8±0.5) | 30 (6.8±0.5) | 1.0 (–0.4 to 2.4) |
| Cognitive function | | | |
| MoCA score ≥26 | 33 (8.2±0.5) | 34 (7.0±0.5) | 1.2 (0 to 2.4) |
| MoCA score <26 | 114 (7.9±0.3) | 119 (6.3±0.3) | 1.6 (0.9 to 2.2) |
| Frailty status | | | |
| Nonfrail or prefrail | 72 (7.9±0.3) | 69 (7.2±0.3) | 0.7 (–0.1 to 1.5) |
| Frail | 77 (8.1±0.3) | 86 (6.0±0.3) | 2.1 (1.3 to 2.8) |

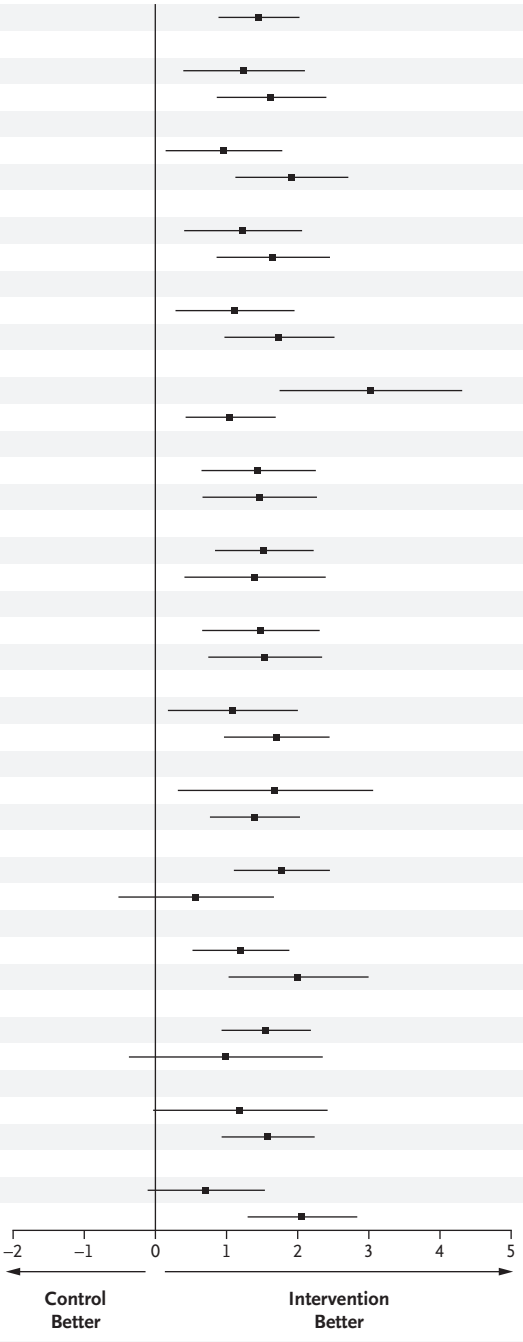



**Figure 3. Prespecified Subgroup Analysis of the Primary Outcome.**

Plus–minus values are least-squares mean ±SE scores on the Short Physical Performance Battery (SPPB). The primary outcome was the score on the SPPB (total scores range from 0 to 12, with lower scores indicating more severe physical dysfunction) at 3 months. The effect size of the intervention on the SPPB score was relatively large and uniform across a broad range of key subgroups. The widths of the confidence intervals have not been adjusted for multiple comparisons, so the intervals should not be used to infer definitive treatment effects for the subgroups. Race was reported by the patient. An ejection fraction of at least 45% indicates preserved ejection fraction. The body-mass index (BMI) is the weight in kilograms divided by the square of the height in meters. Cognitive function was assessed with the use of the Montreal Cognitive Assessment (MoCA); scores range from 0 to 30, with higher scores indicating better cognitive function, and a score of 26 or higher indicates normal cognitive function. COPD denotes chronic obstructive pulmonary disease, and NYHA New York Heart Association.

respect to 6-minute walk distance, rehospitalization, and death, but adherence to the intervention was low (43%).[25]

Physical dysfunction, frailty, and depression are often unrecognized clinically in older patients hospitalized for heart failure,[8,28] are generally not addressed in clinical care pathways,[10,29] and probably contribute to delayed, incomplete recovery and high rates of rehospitalization, death, and long-term loss of independence after hospital discharge.[2,11,12,14] Physical-function impairments in the patients in the REHAB-HF trial were broader and more severe than those observed in patients with chronic heart failure.[28] For example, the mean baseline 6-minute walk distance in the REHAB-HF trial was half that observed in the HF-ACTION (Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training) trial,[30] and severe leg weakness prevented nearly one third of the patients from standing even once from a seated position without the use of their arms. The patients in our trial also had severe deficits in balance and mobility, and a history of falls and other geriatric conditions was common — findings that are not typically seen in patients with chronic heart failure and are not addressed by conventional cardiac rehabilitation. The initiation of standard endurance exercise training in frail, older patients without first addressing deficits in balance and mobility can limit efficacy[31] and increase the risk of injuries and falls.[32,33]

The intervention-related benefits seen in the REHAB-HF trial generally exceeded previously reported values for the minimal clinically important difference. The mean difference between the groups in the Short Physical Performance Battery score (1.5 points) was three times as large as the reported minimal clinically important difference (0.5 points).[21,34] All three of the components of the Short Physical Performance Battery — corresponding to balance, strength, and mobility — showed greater improvement in the intervention group than in the control group. The apparent benefits in 6-minute walk distance (34 m) and KCCQ score (7.1 points) were also larger than the reported minimal clinically important differences (30 m and 5 points, respectively).[35,36] The suggested benefit for depression is of interest, since depression is common among patients with heart failure and is associated with frequent rehospitalization,[37] and trials targeting depression in patients with heart failure have had neutral results.

The greater improvements in physical function relative to the control group were seen despite the receipt of routine physical or occupational therapy or traditional cardiac or pulmonary rehabilitation as part of usual care by 43% of the patients in the control group. At 6 months, 83% of the patients in the intervention group who were alive and were being followed by telephone contact reported regular home exercise, which suggested that behavioral change — a requisite for long-term adherence — may have occurred.

The intervention-related benefits may be related to both the severity of the baseline deficits and the robust, broad systemic effects of physical exercise, which favorably alters energy metabolism, oxidative stress, inflammation, tissue repair, growth-factor response, and regulatory pathways.[38] Older patients with heart failure can have severe skeletal-muscle myopathy that contributes to physical dysfunction and abates with exercise.[9]

The number of deaths, including deaths from cardiovascular causes, was higher in the intervention group than in the control group, although the numbers and differences were small and may have been due to chance. A meta-analysis of trials of exercise-based rehabilitation for heart failure showed no significant effect on death from any cause during follow-up for up to 12 months.[39] In the EJECTION-HF trial, fewer deaths were reported in the intervention group than in the control group at 12 months.[25] Given the wide confidence interval for the rate ratio for death from any cause, we cannot rule out the possibility of an increase (or decrease) in risk with an early exercise regimen among some patients.

Our trial has other important limitations. First, the results did not show a beneficial effect on clinical events. However, a study that examined patient preferences in patients with heart failure indicated that improving physical function and maintaining independence are highly valued, independent of clinical events.[40] Second, although the staff members who assessed the primary outcome were unaware of the trial-group assignments, it was not possible for patients to be unaware of the group to which they had been randomly assigned. Third, the benefits of the intervention over usual care may have been moderated owing to the usual-care exercise

therapy received by the control group. Fourth, differences between the groups in the amount of caregiver attention could have influenced outcomes. Fifth, the long-term durability of the benefit of the intervention is uncertain. Finally, many patients were ineligible or unable or unwilling to participate, and some discontinued the intervention.

Among patients who were hospitalized for acute decompensated heart failure, a transitional, tailored, progressive rehabilitation intervention that included multiple physical-function domains and that began during, or early after, hospitalization and continued for 12 weeks after hospital discharge resulted in significantly greater improvement in physical function than usual care.

Supported by research grants from the National Institutes of Health (R01AG045551, R01AG18915, P30AG021332, P30AG028716, and U24AG059624), the Kermit Glenn Phillips II Chair in Cardiovascular Medicine, and the Oristano Family Fund at Wake Forest School of Medicine.

Dr. Kitzman reports receiving steering committee fees and data and safety monitoring board fees from AbbVie, grant support, paid to Wake Forest Baptist Health, and advisory board fees from AstraZeneca and Bayer, advisory board fees from Boehringer Ingelheim and Corvia Medical, consulting fees from Keyto and Merck, and grant support, paid to Wake Forest Baptist Health, and consulting fees from Novartis; Dr. Whellan, receiving grant support, paid to Thomas Jefferson University, from Amgen, end-point committee fees from CVRx and FibroGen, steering committee fees from Cytokinetics, and grant support, paid to Thomas Jefferson University, and advisory board fees from Novo Nordisk; Dr. Duncan, owning stock in Care Directions; and Dr. Mentz, receiving grant support from American Regent and Cytokinetics, consulting fees from Amgen, Boehringer Ingelheim, and Relypsa, research support and honoraria from Abbott, American Regent, Amgen, Boehringer Ingelheim, Eli Lilly, Boston Scientific, Cytokinetics, FAST BioMedical, Gilead Sciences, Innolife, Medtronic, Relypsa, Respicardia, Roche, Sanofi, Vifor Pharma, and Windtree Therapeutics, grant support, research support, and honoraria from AstraZeneca, and research support, consulting fees, and honoraria from Bayer, Merck, and Novartis. No other potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

A data sharing statement provided by the authors is available with the full text of this article at NEJM.org.

We thank Alain Bertoni, M.D., Peter Brubaker, Ph.D., and Jack Rejeski, Ph.D. for their critical review and editing of an earlier version of the manuscript; and Timothy Morgan, Ph.D. (deceased), for his biostatistical expertise.

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