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ORIGINAL RESEARCH

Atrial Fibrillation Status and Physical Rehabilitation in Older Patients With Acute Decompensated Heart Failure: An Analysis From the REHAB-HF Trial

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BACKGROUND: The REHAB-HF (Rehabilitation Therapy in Older Acute Heart Failure Patients) trial demonstrated that a transitional, tailored, progressive rehabilitation intervention improved physical function, 6-minute walk distance, frailty, quality-of-life, and depression in older patients hospitalized for acute decompensated heart failure. This analysis assessed the impact of atrial fibrillation (AF) on intervention benefits.

METHODS AND RESULTS: Of 349 enrolled patients hospitalized for acute decompensated heart failure (mean age 72.7±8.1 years), 176 (50.4%) had AF. Participants were randomly assigned to 12-week rehabilitation intervention or attention control. The primary outcome was Short Physical Performance Battery score at 3 months. Participants with AF were older (74.4±8.3 versus 70.8±7.5, $P<0.0001$) and had higher prevalence of heart failure with preserved ejection fraction (58.5% versus 47.4%, $P=0.037$). Patients with and without AF had similar improvement in Short Physical Performance Battery score (mean difference between rehabilitation intervention and attention control, 1.5 [95% CI, 0.6–2.3] versus 1.5 [95% CI, 0.7–2.3]; $P<0.001$). Those with AF had significant improvement in 6-minute walk distance (all $P<0.05$) and each of the Short Physical Performance Battery domains: balance, 4-meter walk, and chair rise. Kansas City Cardiomyopathy Questionnaire score significantly improved in patients with AF ($P<0.05$) but not those without AF ($P>0.05$). Interaction *P* values for 3-month outcomes by AF status were not significant ($P>0.1$). No significant differences were observed in deaths, all-cause rehospitalizations, or heart failure hospitalizations at 6 months.

CONCLUSIONS: In older, hospitalized patients with acute decompensated heart failure, the presence of AF did not significantly affect the benefit of the rehabilitation intervention on physical function and quality of life. The intervention appears safe and effective regardless of AF status.

REGISTRATION: URL: https://www.clinicaltrials.gov; Unique Identifier: NCT02196038.

Key Words: arrhythmia ■ atrial fibrillation ■ frailty ■ heart failure ■ rehabilitation intervention

Atrial fibrillation (AF) and heart failure (HF) are associated with increased morbidity and mortality and, when diagnosed in the same individual, lead to worse outcomes than either condition alone.[1–3] There is a growing prevalence of both conditions, and it is estimated that by 2030, 12 million Americans will be affected by AF, and more than 8 million will be diagnosed with HF.[4,5] AF has been associated with reduced exercise capacity in both patients with HF with reduced ejection fraction (EF) and patients with HF with

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RESEARCH PERSPECTIVE

What Is New?

- In older patients hospitalized with acute decompensated heart failure, the presence of atrial fibrillation did not significantly affect the benefits of a novel, transitional, tailored, progressive rehabilitation intervention on physical function and quality of life.

What Question Should Be Addressed Next?

- Future studies should determine if the degree of atrial fibrillation burden impacts the response to exercise-based rehabilitation in patients with heart failure.
- Trials powered to detect differences in mortality and rehospitalization between heart failure patients with and without atrial fibrillation undergoing rehabilitation are needed to fully assess the impact of rhythm status on the long-term efficacy of such interventions.

Nonstandard Abbreviations and Acronyms

ADHF	acute decompensated heart failure
KCCQ	Kansas City Cardiomyopathy Questionnaire
SPPB	Short Physical Performance Battery

preserved EF.[6,7] This decreased exercise capacity is likely influenced by left atrial structural remodeling, with greater degrees of remodeling associated with diminished exercise capacity.[8] Additionally, factors such as elevated left ventricular filling pressures, impaired chronotropic response, and reduced contractile reserve are associated with lower exercise capacity in patients with both AF and concurrent HF with preserved EF.[9] Given the underlying pathophysiology, coupled with the prevalence of AF in older patients and its correlation with increased frailty, it is reasonable to suspect that this population may experience less benefit from rehabilitation interventions compared with those without AF. We sought to investigate the role AF plays in exercise capacity and rehabilitation potential among patients with HF.

Exercise training has been evaluated in both patients with AF and patients with HF. The implementation of regular exercise training in patients with AF has been found to be safe, reduce AF recurrence, and improve cardiorespiratory fitness and quality of life (QOL).[10] The CARDIO-FIT Study, a randomized study of aerobic interval training in patients with AF, found that AF burden and symptom severity decreased with improvement in cardiorespiratory fitness following a supervised exercise program.[11] The largest randomized trial to study standardized exercise therapy in patients with chronic HF (HF-ACTION [Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training]) demonstrated that those with AF and chronic HF were of older age, had reduced exercise capacity at baseline, and were more likely to suffer clinical events.[12,13] Despite concerns about the safety and efficacy of exercise in patients with AF, patients with HF with reduced EF and AF experienced a similar benefit from participating in exercise training as patients with HF with reduced EF and sinus rhythm.[12] Overall, protective benefits of moderate levels of physical activity are associated with reduced mortality, cardiovascular morbidity, and stroke in patients with AF.[10,12,14] It is unknown if these benefits would affect clinical outcomes in hospitalized patients with acute decompensated heart failure (ADHF) who have AF.

Cardiac rehabilitation can occur over the course of several weeks after a recent hospitalization depending on an institution's protocol. Rehabilitation generally involves scheduled exercise training, which can focus on several goals, including strength, balance, mobility, or endurance. It has been established that regular aerobic exercise has been associated with lower AF incidence in older adults.[15] A study by Malmo et al demonstrated that a 12-week cardiac rehabilitation program that included aerobic interval training 3 times a week significantly decreased time in AF for those with both permanent and paroxysmal AF. The program also improved AF symptoms, exercise capacity, and QOL.[16]

The multicenter, randomized REHAB-HF (Rehabilitation Therapy in Older Acute Heart Failure Patients) trial demonstrated that a transitional, tailored, progressive, and multidomain physical rehabilitation intervention targeting older patients hospitalized with ADHF led to significant improvement in both physical function and QOL.[17] This prespecified secondary analysis of the REHAB-HF trial was done to assess for physical and clinical differences in outcome among patients with and without a diagnosis of AF at enrollment.

METHODS

Study Design and Population

The data that support the findings of this study are available from the corresponding author upon reasonable request. The details of the REHAB-HF trial design, the physical rehabilitation intervention, and primary trial results have been published previously.[17–19] Briefly, the REHAB-HF trial was a multicenter, randomized, attention-controlled trial of a 12-week early, progressive rehabilitation intervention in patients ≥60 years of age hospitalized for ADHF. The institutional review boards at each enrolling site approved the study. All patients provided written informed consent. This study followed the Consolidated Standards of Reporting Trials reporting guideline. Key inclusion criteria were, before admission, patient was independent with basic activities of daily living, including the ability to ambulate independently, not living in a nursing home or assisted living, and an expectation for patients to be discharged home. Exclusion criteria included end-stage HF (including continuous inotropes or ventricular assist device anticipated within the next 6 months), end-stage kidney disease on dialysis, significant dementia, or otherwise inability to participate in the rehabilitation intervention. Patients were randomized 1:1 to either rehabilitation intervention or attention control. Baseline AF status was determined at the time of enrollment at the index hospitalization based on electronic medical record review and documentation. Patients were divided based on status (AF versus no AF) for the primary, prespecified analysis.

Study Intervention

The study intervention was an early, transitional, tailored, progressive, multidomain physical rehabilitation program that was focused on strength, balance, mobility, and endurance, all of which were aimed at addressing common deficits observed in an older population with ADHF.[18,19] The intervention was initiated as soon as safely possible after hospital admission and continued in an outpatient facility after discharge. The outpatient sessions lasted 60 minutes each, 3 days weekly for 12 weeks (approximately 36 sessions). After the participant's home environment was assessed by a study staff visit, the outpatient sessions were complemented by low-intensity home exercise on nonfacility days. At the 3-month visit, participants were transitioned into the independent maintenance phase for months 4 to 6. The participants were given individualized exercise prescriptions and subsequently followed up every 4 weeks by telephone. Patients randomly assigned to the attention control group received a telephone call every 2 weeks and were encouraged to adhere to usual-care therapy and scheduled follow-up appointments. However, they did not receive specific recommendations with respect to exercise. Patients in both arms of the study had in-person study visits at 1 month and 3 months from the initial hospitalization. Patients were followed for a total of 6 months.

Outcomes of Interest

The primary outcome was the SPPB at 3-month follow-up. The SPPB is a standardized and reproducible measure of global physical function in older people and predicts several clinical outcomes.[20,21] There are 3 main components: balance, gait speed, and strength (repeated chair rise). Each component is scored from 0 to 4, and lower total SPPB scores indicate worse physical function. Other outcomes of interest at 3 months include 6-minute walk distance, QOL as assessed by the Kansas City Cardiomyopathy Questionnaire (KCCQ), health status assessed by the EuroQoL visual analog scale, depression by the Geriatric Depression Scale-15, frailty by modified Fried criteria, and cognition by the Montreal Cognitive Assessment. All assessments were obtained by blinded assessors. Clinical outcomes of interest at 6 months included all-cause rehospitalization, combined all-cause rehospitalization and death, HF-specific rehospitalizations, death, and falls. The results of the intervention arm in the overall REHAB-HF trial have been previously published.[17]

Statistical Analysis

Baseline participant characteristics were reported by AF status and intervention groups. Mean±SD or median (interquartile range) were reported for continuous variables and N (%) for categorical variables. Participant characteristics were compared across groups using Student's *t* test for continuous variables and chi-square tests for categorical variables.

To evaluate the potential effect of AF status on the effect of the intervention on 3-month outcomes (SPPB, 6-minute walk distance, gait speed, grip strength, KCCQ, modified Fried criteria, EuroQoL visual analog scale, Geriatric Depression Scale-15, Montreal Cognitive Assessment), we used general linear models that included indicator variables for intervention, AF status, and their interaction. All analyses were adjusted for baseline measure, age, sex, clinical site, and EF category of <45% or ≥45%, as in other REHAB-HF analyses. We used least square means to estimate the effects of the intervention in patients by AF status. The effect sizes were reported as mean differences between those 2 intervention groups with 95% CIs.

The moderating effect of AF status group on the effect of the intervention on 6-month clinical outcomes was assessed using Poisson regression for number of all-cause rehospitalizations, HF rehospitalizations, death, and combined all-cause rehospitalization and deaths, using logistic regression for proportion of patients with falls. All analyses were adjusted for age, sex, clinical site, and EF category. All-cause rehospitalization was also adjusted for baseline SPPB score as prespecified. Effect sizes for the AF status subgroups were summarized as rate ratio for count-based outcomes and odds ratio for binary outcomes. A *P* value of <0.05 was determined to be

Table 1. Baseline Characteristics of Patients by Atrial Fibrillation Status

Atrial fibrillation status							
	Yes			No			
Characteristics	All (N=176)	Rehabilitation intervention (N=89)	Attention control (N=87)	All (N=173)	Rehabilitation intervention (N=86)	Attention control (N=87)	*P* value
Age, y	74.4±8.3	75.4±8.6	73.5±7.9	70.8±7.5	70.7±7.7	71.0±7.3	<0.0001
Female sex	84 (47.7)	39 (43.8)	45 (51.7)	99 (57.2)	46 (53.5)	53 (60.9)	0.0757
White race	111 (63.1)	56 (62.9)	55 (63.2)	66 (38.2)	38 (44.2)	28 (32.2)	<0.0001
Education level							0.0022
Less than HS	30 (17.0)	17 (19.1)	13 (14.9)	30 (17.3)	18 (20.9)	12 (13.8)	
HS or equivalent	65 (36.9)	28 (31.5)	37 (42.5)	93 (53.8)	44 (51.2)	49 (56.3)	
≥College	81 (46.0)	44 (49.4)	37 (42.5)	50 (28.9)	24 (27.9)	26 (29.9)	
Living arrangement							0.0287
Alone	52 (29.7)	32 (36.4)	20 (23.0)	56 (32.7)	24 (28.2)	32 (37.2)	
With spouse or family member	112 (64.0)	52 (59.1)	60 (69.0)	91 (53.2)	47 (55.3)	44 (51.2)	
With friend or caregiver	11 (6.3)	4 (4.5)	7 (8.0)	24 (14.0)	14 (16.5)	10 (11.6)	
Body mass index (kg/m^2)	32.6±8.0	32.4±7.5	32.7±8.6	33.1±9.0	33.3±8.9	32.9±9.1	0.5466
Baseline weight (kg)	94.3±25.2	95.2±24.7	93.3±25.9	93.3±24.9	94.3±24.0	92.3±25.8	0.7019
Baseline heart rate, bpm	77.9±15.5	79.4±16.2	76.3±14.8	77.6±16.2	78.1±19.0	77.1±12.9	0.8640
Ejection fraction ≥45%	103 (58.5)	52 (58.4)	51 (58.6)	82 (47.4)	41 (47.7)	41 (47.1)	0.0374
New York Heart Association							0.6254
I–II	37 (21.0)	17 (19.1)	20 (23.0)	30 (17.3)	17 (19.8)	13 (14.9)	
III	92 (52.3)	51 (57.3)	41 (47.1)	98 (56.6)	49 (57.0)	49 (56.3)	
IV	47 (26.7)	21 (23.6)	26 (29.9)	45 (26.0)	20 (23.3)	25 (28.7)	
B-type natriuretic peptide, pg/mL	500.5 (290.0–952.0)	525.0 (300.0–936.0)	479.0 (276.0–987.0)	687.5 (330.0–1367.0)	739.0 (482.0–1314.0)	636.7 (246.0–1367.0)	0.0504
N-terminal pro-B-type natriuretic peptide, pg/mL	3065.0 (1492.0–5933.0)	3131.0 (1492.0–10023.0)	2969.5 (1622.5–5041.5)	3446.0 (1510.0–6507.0)	4441.0 (1939.0–8351.0)	2488.0 (844.0–4858.0)	0.7446
Index hospital length of stay, d	5.0 (3.0–7.0)	5.0 (3.0–7.0)	5.0 (3.0–7.0)	5.0 (3.0–6.0)	4.0 (3.0–6.0)	5.0 (3.0–7.0)	0.2356
Prior hospitalization past 6 mo	82 (46.6)	38 (42.7)	44 (50.6)	74 (42.8)	38 (44.2)	36 (41.4)	0.4734
CHADS2VASc score	4.8±1.5	4.9±1.5	4.8±1.5	4.6±1.3	4.7±1.4	4.6±1.3	0.2778
Comorbidities							
Hypertension	161 (91.5)	80 (89.9)	81 (93.1)	160 (92.5)	79 (91.9)	81 (93.1)	0.7288
Myocardial infarction	35 (19.9)	17 (19.1)	18 (20.7)	28 (16.2)	14 (16.3)	14 (16.1)	0.3687
Coronary revascularization	55 (31.3)	30 (33.7)	25 (28.7)	47 (27.2)	25 (29.1)	22 (25.3)	0.4018
Diabetes	83 (47.2)	50 (56.2)	33 (37.9)	103 (59.5)	53 (61.6)	50 (57.5)	0.0205
Hyperlipidemia	118 (67.0)	56 (62.9)	62 (71.3)	112 (64.7)	54 (62.8)	58 (66.7)	0.6496
Chronic obstructive pulmonary disease	51 (29.0)	28 (31.5)	23 (26.4)	47 (27.2)	26 (30.2)	21 (24.1)	0.7068

(Continued)

Table 1. Continued

Atrial fibrillation status							
	Yes			No			
Characteristics	All (N=176)	Rehabilitation intervention (N=89)	Attention control (N=87)	All (N=173)	Rehabilitation intervention (N=86)	Attention control (N=87)	*P* value
Chronic kidney disease	54 (30.7)	24 (27.0)	30 (34.5)	63 (36.4)	35 (40.7)	28 (32.2)	0.2565
Stroke	27 (15.3)	12 (13.5)	15 (17.2)	25 (14.5)	14 (16.3)	11 (12.6)	0.8154
Peripheral vascular disease	20 (11.4)	12 (13.5)	8 (9.2)	20 (11.6)	15 (17.4)	5 (5.7)	0.9539
Arthritis	69 (39.2)	38 (42.7)	31 (35.6)	85 (49.1)	46 (53.5)	39 (44.8)	0.0618
Liver disease	11 (6.3)	4 (4.5)	7 (8.0)	3 (1.7)	2 (2.3)	1 (1.1)	0.0316
Cancer	41 (23.3)	23 (25.8)	18 (20.7)	34 (19.7)	19 (22.1)	15 (17.2)	0.4075
Sleep apnea	64 (36.4)	31 (34.8)	33 (37.9)	61 (35.3)	37 (43.0)	24 (27.6)	0.8298
Depression	33 (18.8)	15 (16.9)	18 (20.7)	29 (16.8)	14 (16.3)	15 (17.2)	0.6273
Dementia	5 (2.8)	3 (3.4)	2 (2.3)	5 (2.9)	3 (3.5)	2 (2.3)	0.978
Geriatric conditions							
Baseline frailty							0.1361
Nonfrail	7 (4.0)	5 (5.6)	2 (2.3)	5 (2.9)	1 (1.2)	4 (4.6)	
Prefrail	64 (36.4)	31 (34.8)	33 (37.9)	81 (46.8)	46 (53.5)	35 (40.2)	
Frail	105 (59.7)	53 (59.6)	52 (59.8)	87 (50.3)	39 (45.3)	48 (55.2)	
Urinary incontinence	26 (18.2)	13 (18.6)	13 (17.8)	14 (9.8)	6 (8.1)	8 (11.6)	0.0408
Fall in previous 3 mo	22 (15.2)	11 (15.3)	11 (15.1)	22 (15.3)	13 (17.6)	9 (12.9)	0.9801
Heart failure therapies at discharge							
Loop diuretic	167 (95.4)	83 (93.3)	84 (97.7)	159 (91.9)	79 (91.9)	80 (92.0)	0.1772
Beta blocker	130 (74.3)	62 (69.7)	68 (79.1)	146 (84.4)	76 (88.4)	70 (80.5)	0.02
Angiotensin-converting enzyme inhibitor	60 (34.3)	32 (36.0)	28 (32.6)	71 (41.0)	33 (38.4)	38 (43.7)	0.1935
Angiotensin receptor blocker	34 (19.4)	15 (16.9)	19 (22.1)	41 (23.7)	23 (26.7)	18 (20.7)	0.3326
Aldosterone antagonist	35 (20.0)	16 (18.0)	19 (22.1)	28 (16.2)	13 (15.1)	15 (17.2)	0.3554
Entresto	1 (0.6)	0 (0.0)	1 (1.2)	1 (0.6)	1 (1.2)	0 (0.0)	0.9935
Digoxin	15 (8.6)	8 (9.0)	7 (8.1)	4 (2.3)	0 (0.0)	4 (4.6)	0.0102
Insulin	38 (21.7)	21 (23.6)	17 (19.8)	61 (35.3)	33 (38.4)	28 (32.2)	0.0051
Oral diabetic medication	46 (26.3)	29 (32.6)	17 (19.8)	39 (22.5)	22 (25.6)	17 (19.5)	0.4165
Anticoagulant	128 (73.1)	64 (71.9)	64 (74.4)	34 (19.7)	19 (22.1)	15 (17.2)	<0.0001
Antiarrhythmics	49 (28.0)	25 (28.1)	24 (27.9)	6 (3.5)	4 (4.7)	2 (2.3)	<0.0001
Calcium channel blocker	43 (24.6)	25 (28.1)	18 (20.9)	50 (28.9)	25 (29.1)	25 (28.7)	0.3614
Automatic implantable cardioverter-defibrillator	36 (20.5)	19 (21.3)	17 (19.5)	25 (14.5)	14 (16.3)	11 (12.6)	0.1398
Biventricular pacemaker	17 (9.7)	7 (7.9)	10 (11.5)	8 (4.6)	5 (5.8)	3 (3.4)	0.0682
Pacemaker	28 (15.9)	11 (12.4)	17 (19.5)	12 (6.9)	8 (9.3)	4 (4.6)	0.0085

n (%) for categorical variable, mean±SD for continuous variable, median (Q1–Q3) for skewed continuous variable.

statistically significant for overall comparisons. The interaction between AF status and the intervention arm was determined to be significant for *P*<0.10. In this exploratory analysis the *P* values and the widths of the CIs were not adjusted for multiple comparisons. Therefore, the intervals should not be used to infer definitive treatment effects.

RESULTS

Baseline Characteristics

AF was prevalent in 176 of the 349 trial participants (50.4%). Baseline characteristics differed among participants by AF status (Table 1). Compared with patients who did not have a diagnosis of AF at index hospitalization, participants with AF were older (74.4±8.3 versus 70.8±7.5, *P*<0.0001), were more likely to be White (63.1% versus 38.2%, *P*<0.0001), and had an increased likelihood of having HF with preserved EF (58.5% versus 47.4%, *P*=0.0374). Diabetes was more prevalent in patients without AF (59.5% versus 47.2%, *P*=0.0205), but other cardiac comorbidities were not significantly different between subgroups.

Participants with AF were more likely to have a pacemaker (15.9 versus 6.9%, *P*=0.0085) and to be prescribed anticoagulation (73.1% versus 19.7%, *P*<0.0001), antiarrhythmic therapy (28% versus 3.5%, *P*<0.0001), and digoxin (8.6% versus 2.3%, *P*=0.0102) when compared with participants who did not have AF. Participants without AF were more likely to be prescribed a β blocker (84.4% versus 74.3%, *P*=0.0200).

Physical Function and Quality of Life Outcomes by Atrial Fibrillation Status

Baseline QOL and physical function scores did not differ significantly between the 2 AF status groups (Table 2). Both groups had similar SPPB scores, 6-minute walk distance, gait speed, and KCCQ scores. However, some differences were noted. Physical function and QOL outcomes at 3 months are presented in Table 3. Patients with AF undergoing the rehabilitation intervention showed a significant increase in the SPPB score compared with controls. Patients with and without AF had similar improvement in SBPP score (mean difference between rehabilitation intervention and attention control, 1.5 [95% CI, 0.6–2.3] versus 1.5 [95% CI, 0.7–2.3]; *P*<0.001). There was no significant difference in mean SPPB between the 2 groups with and without AF (*P*=0.98). Significant improvements were also seen in balance, 4-meter walk, chair rise, 6-minute walk distance, gait speed, and overall KCCQ score in patients with AF (*P*<0.05). The interaction *P* values for the 3-month outcomes by AF status were not significant (*P*>0.1), with similar improvements seen in SPPB

Table 2. Baseline Functional Performance by Atrial Fibrillation Status

Characteristics	Atrial fibrillation status						P value
	Yes			No			
	All	Rehabilitation intervention	Attention control	All	Rehabilitation intervention	Attention control	
Short Physical Performance Battery score	5.9±2.7	6.0±2.8	5.9±2.7	6.2±2.7	6.1±2.8	6.4±2.5	0.3292
Balance	2.6±1.3	2.6±1.3	2.6±1.3	2.6±1.3	2.5±1.4	2.7±1.3	0.7789
4-m walk	2.3±1.1	2.3±1.0	2.3±1.1	2.3±1.0	2.3±1.1	2.3±0.9	0.8798
Chair rise	1.0±1.1	1.1±1.1	1.0±1.2	1.3±1.2	1.2±1.2	1.3±1.2	0.0715
6-min walk distance, m	190.0±109.8	193.4±109.2	186.6±110.9	196.5±100.6	193.8±97.9	199.0±103.6	0.5722
Gait speed, m/s	0.60±0.24	0.59±0.23	0.60±0.25	0.61±0.21	0.60±0.22	0.62±0.19	0.6415
Male grip strength, kg	29.7±10.1	30.0±10.4	29.4±9.8	31.3±10.0	30.7±8.5	32.0±11.7	0.3267
Female grip strength, kg	18.9±7.1	19.5±7.6	18.4±6.7	21.1±6.6	21.7±6.9	20.6±6.5	0.0308
Modified Fried frailty score	2.5±1.1	2.4±1.2	2.5±1.0	2.2±1.1	2.1±1.0	2.3±1.1	0.0447
KCCQ score overall	39.8±21.0	40.9±21.6	38.7±20.5	41.9±20.1	39.4±19.6	44.4±20.4)	0.3608
KCCQ score clinical	40.6±21.0	41.8±21.3	39.3±20.8	41.1±21.1	38.6±21.2	43.6±20.9	0.8293
EuroQol visual analog scale score	57.2±22.2	56.6±24.7	57.8±19.5	59.3±21.1	60.0±19.8	58.5±22.5	0.3669
Cognition (Montreal Cognitive Assessment score)	21.7±4.7	21.9±4.6	21.4±4.8	22.0±4.0	21.9±3.8	22.1±4.3	0.4415
Depression (GDS-15 score)	4.8±3.4	4.6±3.4	5.1±3.3	4.5±3.4	4.8±3.2	4.3±3.5	0.4588

Presented as mean±SD. KCCQ scores range from 0 to 100, with higher score meaning better health status. MoCA score ranges 0 to 30, with higher score meaning better cognitive function. GDS-15 score ranges 0 to 15, with higher score meaning worse depressive symptoms. *P* value for difference between atrial fibrillation status groups. GDS-15 indicates Geriatric Depression Scale-15; and KCCQ, Kansas City Cardiomyopathy Questionnaire.

Table 3. Physical Function Outcomes at 3 Months by Atrial Fibrillation Status

Outcome	Atrial fibrillation status								P for interaction
	Yes				No				
	RI (n=77)	AC (n=75)			RI (n=72)	AC (n=80)			
	Mean (SE)	Mean (SE)	Effect size* (CI)	P for difference	Mean (SE)	Mean (SE)	Effect size* (CI)	P for difference	
Short Physical Performance Battery score	7.7 (0.3)	6.2 (0.3)	1.5 (0.7 to 2.3)	0.0004†	8.2 (0.3)	6.7 (0.3)	1.5 (0.6 to 2.3)	0.0004	0.9793
Balance	3.1 (0.1)	2.7 (0.1)	0.4 (0.0 to 0.8)	0.0348†	3.1 (0.1)	2.8 (0.1)	0.3 (−0.0 to 0.7)	0.0867	0.7783
4-m walk	2.8 (0.1)	2.3 (0.1)	0.5 (0.2 to 0.8)	0.0019†	3.0 (0.1)	2.6 (0.1)	0.4 (0.1 to 0.7)	0.0118	0.6718
Chair rise	1.9 (0.1)	1.3 (0.1)	0.6 (0.3 to 1.0)	0.0004†	2.0 (0.1)	1.4 (0.1)	0.6 (0.3 to 1.0)	0.0005	0.9561
6-min walk distance, m	282.8 (12.9)	248.0 (13.7)	34.8 (3.0 to 66.6)	0.0321†	284.1 (12.9)	251.6 (12.3)	32.4 (0.8 to 64.0)	0.0445	0.9157
Gait speed, m/s	0.78 (0.02)	0.68 (0.03)	0.10 (0.04 to 0.17)	0.0012†	0.82 (0.02)	0.69 (0.02)	0.13 (0.07 to 0.19)	<0.0001	0.5531
Male grip strength, kg	30.3 (1.1)	30.9 (1.2)	−0.6 (−3.5 to 2.3)	0.6777	29.8 (1.2)	30.1 (1.2)	−0.3 (−3.4 to 2.8)	0.8437	0.8882
Female grip strength, kg	21.8 (1.1)	22.4 (1.0)	−0.6 (−3.0 to 1.7)	0.5917	21.3 (0.9)	21.1 (0.9)	0.2 (−2.0 to 2.4)	0.8537	0.602
Modified Fried frailty score	1.5 (0.1)	1.8 (0.2)	−0.3 (−0.6 to 0.1)	0.1153	1.4 (0.1)	1.7 (0.1)	−0.3 (−0.6 to 0.1)	0.1453	0.9335
KCCQ score overall	68.0 (2.9)	58.9 (3.0)	9.1 (1.8 to 16.5)	0.0151†	67.5 (2.9)	62.4 (2.8)	5.1 (−2.2 to 12.5)	0.1724	0.4477
KCCQ score clinical	68.5 (2.9)	60.3 (3.0)	8.2 (0.9 to 15.6)	0.0289†	66.8 (2.9)	63.7 (2.8)	3.1 (−4.3 to 10.5)	0.4084	0.3347
EuroQol visual analog scale score	69.7 (2.7)	62.1 (2.8)	7.5 (0.8 to 14.2)	0.0282†	71.1 (2.6)	64.6 (2.5)	6.4 (−0.3 to 13.1)	0.0599	0.8218
Cognition (Montreal Cognitive Assessment score)	22.4 (0.5)	23.2 (0.5)	−0.8 (−2.0 to 0.4)	0.1774	22.5 (0.4)	22.2 (0.4)	0.3 (−0.8 to 1.5)	0.5877	0.1782
Depression (Geriatric Depression Scale-15 score)	3.6 (0.3)	4.5 (0.4)	−0.9 (−1.8 to −0.0)	0.0416	3.5 (0.3)	4.1 (0.3)	−0.6 (−1.4 to 0.3)	0.194	0.6038

AC indicates attention control; KCCQ, Kansas City Cardiomyopathy Questionnaire; and RI, rehabilitation intervention.
*Effect sizes are reported as difference between means of RI and AC groups with 95% confidence intervals.
†*P* value for difference between atrial fibrillation and non-atrial fibrillation groups.

score, 6MWD, gait speed, and KCCQ score regardless of AF subgrouping.

Clinical Event Outcomes at 6 Months by Atrial Fibrillation Status

The rehabilitation intervention did not significantly reduce all-cause rehospitalizations, deaths, or HF rehospitalizations in either patients with or without AF. Among patients with and without AF, there was no significant interaction by AF status for clinical outcomes at 6 months (interaction *P* values >0.1) (Table 4). Very few cardioversions or ablations occurred during the trial period (Table 4).

DISCUSSION

Our main finding from this analysis of the REHAB-HF trial showed that older adults hospitalized for ADHF with or without AF significantly improved physical function using a transitional, tailored, progressive rehabilitation intervention. The unique intervention in REHAB-HF focused on strength, balance, mobility, and endurance. Patients with AF and ADHF were comparatively older and were prescribed more therapies, such as antiarrhythmics. These patients had similar baseline quality of life and physical function compared with patients with ADHF who did not have AF. Consistent with previous studies that identified a benefit of cardiac rehabilitation for patients with AF and HF with reduced EF in the outpatient setting, patients with ADHF and AF derive similar benefits from the intervention as patients without AF.

We hypothesized that patients with AF and ADHF would have significant improvements in physical function outcomes compared with patients with ADHF alone. This would suggest that AF could be independently improved by this intervention. Prior interventions in patients with AF, including typical cardiac rehabilitation, aerobic exercises, and yoga, have shown improvements.[22–24] To varying degrees, studies have shown a reduction in AF burden, lower AF recurrence, and improved QOL.[10,11] Although AF seems to be a targetable HF comorbidity with physical interventions, this substudy was unable to find a significant difference when stratifying by the arrhythmia.

There were expected differences between our baseline groups. Antiarrhythmic drug use, digoxin use, and pacemakers were significantly more prevalent in the group with AF.[25,26] This is somewhat expected as recent trends in AF treatment support early initiation of specific therapies.[26,27] The presence of a pacemaker can have a highly variable impact on exercise tolerance depending on the type of device, number of leads, and specific programming.[27,28] AF-specific therapies may affect physical functioning uniquely, which would

Table 4. Clinical Outcomes at 6 Months by Atrial Fibrillation Status

Outcome	Atrial fibrillation status: Yes				No				P for interaction
	Rehab intervention	Attention control	Effect size (CI)	*P* for difference	Rehab intervention	Attention control	Effect size (CI)	*P* for difference	*P* for interaction
All-cause rehospitalizations*	100 (1.19)	114 (1.36)	0.90 (0.68–1.18)	0.4299	94 (1.18)	99 (1.20)	0.94 (0.71–1.25)	0.6872	0.7996
Deaths*	11 (0.13)	8 (0.10)	1.09 (0.43–2.74)	0.8589	10 (0.13)	8 (0.10)	1.32 (0.52–3.40)	0.5598	0.7717
All-cause rehospitalization and death*	111 (1.32)	122 (1.46)	0.90 (0.69–1.16)	0.4193	104 (1.30)	107 (1.29)	0.99 (0.75–1.30)	0.9316	0.6205
Heart failure rehospitalizations*	46 (0.55)	58 (0.69)	0.80 (0.54–1.18)	0.2687	48 (0.60)	52 (0.63)	0.92 (0.62–1.37)	0.6799	0.6287
Falls†	22 (0.25)	33 (0.38)	0.52 (0.27–1.00)	0.0494	26 (0.31)	29 (0.34)	0.87 (0.45–1.66)	0.6669	0.2751
Cardioversion†	3 (0.03)	8 (0.09)	…	…	0 (0.00)	0 (0.00)	…	…	…
Ablation†	6 (0.07)	3 (0.03)	…	…	1 (0.01)	0 (0.00)	…	…	…

Adjusted for clinical site, age, sex, and ejection fraction category (<45% vs ≥45%). All-cause rehospitalization was also adjusted for baseline Short Physical Performance Battery score as prespecified.
*Presented as count (6-month rate) for rehospitalization, deaths, rehospitalizations+deaths, and heart failure rehospitalizations. Effect size is rate ratio (95% CI).
†Presented as count (proportion) for falls, cardioversion, and ablation. Effect size is odds ratio (95% CI) for falls.

require additional studies to assess their individual effect, if any, on the rehabilitation benefits.

This study has several limitations. First, the REHAB-HF trial was not specifically powered to detect differences in the effect of the rehabilitation intervention between patients with and without AF. The subgroup analyses by AF status were prespecified but exploratory. Second, it is not specified whether patients had paroxysmal, persistent, or permanent AF at baseline. This information is unavailable as the original trial did not collect data from ECGs at baseline or subsequent visits on any of the patients in REHAB-HF. AF is a heterogeneous condition, and the variable burden from patient to patient may influence the benefit received from rehabilitation interventions; a patient with paroxysmal AF and a prior single episode may respond differently than another in persistent AF. Third, data on certain medications and therapies were limited, and it is unknown if patients were on optimal doses of rate-controlling agents or antiarrhythmic medications. The interactions of the various treatments for AF on the intervention and vice versa may provide insight into which subgroup of patients may benefit most. Information on AF symptoms, medication changes, or adverse effects of treatments during or after the intervention was similarly unavailable. Fourth, this study enrolled patients during a hospitalization for decompensated HF. Although AF occurs commonly in HF, especially in patients with HF with preserved EF, the overall population of patients with AF is diverse, and this study did not assess if patients with AF alone or AF and different comorbidities would benefit differently. Finally, we did not have echocardiographic data on left atrial size or diastolic function, which could provide further insights into the complex interplay between AF, cardiac remodeling, and exercise capacity in patients with ADHF.

In this cohort of hospitalized patients with ADHF, we did not find a significant difference in performance measures at 3 months or clinical measures at 6 months based on having a baseline diagnosis of AF. Additional studies targeting subgroups within the population with AF are needed to determine if these patients benefit from specific rehabilitation interventions concerning AF symptoms and performance outcomes.

CONCLUSIONS

Among older hospitalized patients with ADHF, participants with AF benefitted equally to those without AF from a transitional, tailored, progressive rehabilitation intervention in terms of physical function and QOL. No change in mortality or rehospitalization rates was noted between the intervention arm and the attention control arm for either participants with or without AF, but the study was not powered to detect this difference. These findings suggest that the rehabilitation intervention is safe to use to improve physical function and QOL in patients hospitalized for ADHF regardless of AF status. Therefore, AF status of patients hospitalized with ADHF should not influence the decision to prescribe rehabilitation.

ARTICLE INFORMATION

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Disclosures

Dr Kitzman has received honoraria outside the present study as a consultant for Bayer, Merck, Medtronic, Relypsa, Merck, Corvia Medical, Boehringer-Ingelheim, NovoNordisk, AstraZeneca, Rivus, Pfizer, and Novartis; grant funding outside the present study from Novartis, Bayer, NovoNordisk, and AstraZeneca; and has stock ownership in Gilead Sciences. Dr Whellan has received research support and consulting fees from Amgen, CVRx, Cytokinetics, Fibrogen, Novartis, and NovoNordisk. The remaining authors have no disclosures to report.

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