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Exercise Training and Implantable Cardioverter-Defibrillator Shocks in Patients With Heart Failure

Results From HF-ACTION (Heart Failure and A Controlled Trial Investigating Outcomes of Exercise TraiNing)

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Objectives The purpose of this study was to determine whether exercise training is associated with an increased risk of implantable cardioverter-defibrillator (ICD) therapy in patients with heart failure (HF).

Background Few data are available regarding the safety of exercise training in patients with ICDs and HF.

Methods HF-ACTION (Heart Failure and A Controlled Trial Investigating Outcomes of Exercise TraiNing) randomized 2,331 outpatients with HF and an ejection fraction (EF) ≤35% to exercise training or usual care. Cox proportional hazards modeling was used to examine the relationship between exercise training and ICD shocks.

Results We identified 1,053 patients (45%) with an ICD at baseline who were randomized to exercise training (n = 546) or usual care (n = 507). Median age was 61 years old, and median EF was 24%. Over a median of 2.2 years of follow-up, 20% (n = 108) of the exercise patients had a shock versus 22% (n = 113) of the control patients. A history of sustained ventricular tachycardia/fibrillation (hazard ratio [HR]: 1.93 [95% confidence interval (CI): 1.47 to 2.54]), previous atrial fibrillation/flutter (HR: 1.63 [95% CI: 1.22 to 2.18]), exercise-induced dysrhythmia (HR: 1.67 [95% CI: 1.23 to 2.26]), lower diastolic blood pressure (HR for 5-mm Hg decrease <60: 1.35 [95% CI: 1.12 to 1.61]), and nonwhite race (HR: 1.50 [95% CI: 1.13 to 2.00]) were associated with an increased risk of ICD shocks. Exercise training was not associated with the occurrence of ICD shocks (HR: 0.90 [95% CI: 0.69 to 1.18], p = 0.45). The presence of an ICD was not associated with the primary efficacy composite endpoint of death or hospitalization (HR: 0.99 [95% CI: 0.86 to 1.14], p = 0.90).

Conclusions We found no evidence of increased ICD shocks in patients with HF and reduced left ventricular function who underwent exercise training. Exercise therapy should not be prohibited in ICD recipients with HF. (Exercise Training Program to Improve Clinical Outcomes in Individuals With Congestive Heart Failure; NCT00047437) (J Am Coll Cardiol HF 2013;1:142–8) © 2013 by the American College of Cardiology Foundation

The implantable cardioverter-defibrillator (ICD) improves survival in patients with heart failure (HF) and significant left ventricular (LV) dysfunction (1,2). Patients with ICDs frequently ask whether they can exercise safely and express fear over receiving a shock (3). Exercise increases catecholamine levels and can provoke both ventricular and supraventricular arrhythmias, which can lead to appropriate and inappropriate shocks (4–6). However, due to the benefits of exercise (7–9), American College of Cardiology/American Heart Association HF guidelines recommend

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exercise training (10). Despite patient concerns and guideline recommendations, few data are available regarding the safety of exercise in HF patients with defibrillators. Previous studies have suggested that exercise may be safe, yet they have been limited by their retrospective nature, small sample size, and limited power (11–13).

The HF-ACTION (Heart Failure and A Controlled Trial Investigating Outcomes of Exercise TraiNing) study randomized patients with symptomatic HF and an LV ejection fraction ≤35% to undergo either an exercise program or receive usual care (9). HF patients randomized to exercise training experienced improved quality of life and functional status. Because over 40% of the HF-ACTION population had an ICD, this trial provides a critical opportunity to evaluate the impact of exercise training on ICD therapy. The objective of this post-hoc analysis was to determine whether exercise training is associated with an increased risk of ICD therapy in patients with HF. We hypothesized that exercise therapy is not associated with an increase in all-cause ICD shocks.

Methods

Study overview. The multicenter, international HF-ACTION trial randomized 2,331 outpatients with HF (New York Heart Association functional classes II to IV) and left ventricular ejection fraction (LVEF) ≤35% to exercise training plus usual care or to usual care alone. The design of the trial has been published previously (9,14). Patients with pacemakers, ICDs, and biventricular pacemakers were eligible for enrollment. Patients were excluded if they were unable to exercise or already engaged in a routine exercise program (>1 session/week) or if they had had a major cardiovascular event in the previous 6 weeks. The randomized treatment consisted of 36 sessions of supervised aerobic exercise training (walking, treadmill, or cycle ergometer) to achieve 60% to 70% target heart rate 3 times/week, followed by home-based exercise training 5 times/week. Patients randomized to the usual care arm were not restricted in terms of their activity. Patients were evaluated every 3 months for the first 2 years and then yearly for 4 years or the end of the trial. After providing informed consent to participate in HF-ACTION, subjects underwent a graded exercise test to evaluate safety and exercise capacity (peak oxygen consumption [Vo_2]).

ICD status and outcomes. For the primary analysis, only patients with an ICD at baseline were included in the ICD exposure group (n = 1,053). A secondary analysis was performed that included all patients with an ICD, including those implanted during follow-up (n = 1,429). For the purpose of this analysis and based upon the case report form, the primary outcome of interest was the occurrence of all-cause ICD shocks (9). ICD interrogation data were not available to classify shocks as either appropriate or inappropriate. However, both appropriate and inappropriate ICD shocks have been associated with increased mortality and impaired quality of life (15–17). HF-ACTION excluded patients if the ICD tachycardia detection limit was set below the target heart rate for exercise training. No data were available regarding ICD programming. All ICD-related care, including tachycardia and bradycardia therapy programming (other than the lower detection limit), were left to the discretion of the patient's physician or electrophysiologist.

Abbreviations and Acronyms

ATP = antitachycardia pacing
CI = confidence interval
EF = ejection fraction
HF = heart failure
HR = hazard ratio
ICD = implantable cardioverter-defibrillator
LV = left ventricular
LVEF = left ventricular ejection fraction
Vo_2 = peak oxygen consumption

Statistical analysis. Baseline characteristics are summarized as median values (25th, 75th percentiles) for continuous variables and percentage (number) for categorical variables.

We used Cox proportional hazards modeling to identify factors independently associated with ICD shocks. All continuous predictors were checked for linearity with outcome, and modifications (usually truncations) were made where necessary. Patients who did not have an ICD at baseline but received one during follow-up were censored at the time of implantation.

Preliminary examination revealed a group of variables completely unrelated to the outcome (all univariate p values >0.8), and they were not considered further. Thus, there were 30 candidate baseline predictors (Table 2) included in the 2-stage modeling process that used backward selection to identify which variables were associated with shock. In stage 1, candidate variables from the HF-ACTION primary endpoint model were considered, and in stage 2, additional candidate variables specific to shock risk were considered. Following the selection process, the randomized therapy was added to the model using an intention-to-treat approach.

A sensitivity analysis was performed using the same methodology in which all patients with an ICD were included (at enrollment and follow-up). Patients who received an ICD during follow-up were left-censored, and values for baseline variables were taken from the follow-up visit closest to the time of ICD implantation.

The composite endpoints: 1) shock or all-cause mortality; and 2) hospitalization or all-cause mortality, were also compared between randomized treatment arms among patients with ICDs at baseline. These comparisons also used Cox proportional hazards models adjusted for established baseline predictors of the endpoints for each analysis. Among patients with an ICD at baseline, the occurrences of the composite endpoint of all-cause mortality, myocardial infarction, or worsening HF were compared between those patients with and without ICD shocks by using a Cox proportional hazards model that included ICD shock as a time-dependent covariate and adjusted for all established baseline predictors of all-cause mortality and cardiovascular death or hospitalization. Changes in peak Vo_2 from baseline

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Table 1 Baseline Characteristics of Patients With ICD at Baseline, by Randomized Therapy

	Exercise Training (n = 546)	Usual Care (n = 507)
Age, yrs	61 (52, 69)	60 (54, 69)
Female	21% (113)	21% (109)
Country		
United States	89% (487)	93% (470)
Canada	7% (40)	5% (25)
France	3% (19)	2% (12)
Race		
Black	24% (128)	25% (124)
White	70% (376)	70% (351)
Other	6% (30)	5% (26)
Body mass index, kg/m^2	30 (26, 34)	29 (26, 34)
Ischemic HF origin	61% (331)	62% (313)
Previous MI	51% (277)	53% (270)
Severe mitral regurgitation	12% (61)	13% (60)
Functional classification		
NYHA class II	57% (312)	57% (291)
NYHA class III/IV	43% (234)	43% (216)
KCCQ summary score	65 (49, 81)	67 (52, 83)
Angina	17% (90)	15% (77)
LVEF	24 (19, 29)	24 (19, 30)
Diabetes	34% (183)	33% (167)
COPD	12% (64)	10% (52)
Hypertension	58% (314)	54% (274)
6-min walk distance, m	366 (287, 433)	369 (293, 427)
Exercise duration on CPX, min	9 (7, 12)	9 (7, 12)
Training heart rate, beats/min	99 (88,109)	96 (86,107)
Peak Vo_2, ml/kg/min	14.1 (11.2, 17.1)	14.1 (11.3, 17.1)
Creatinine clearance (MDRD)	63 (48, 78)	60 (46, 77)
Previous AF/AFL	28% (155)	28% (140)
Previous sustained VT/VF	28% (154)	31% (159)
Beck Depression Inventory II score	9.0 (5.0, 16.0)	8.0 (4.0, 14.0)
Medications		
Beta-blocker	94% (512)	94% (479)
Beta-blocker dose (carvedilol equivalents, mg)	38 (19, 50)	25 (13,50)
Digoxin	49% (270)	54% (273)
ACE inhibitor/ARB	95% (517)	91% (461)
Aldosterone antagonist	53% (288)	50% (253)
Aspirin	64% (351)	63% (321)
Statin	50% (275)	52% (264)
Loop diuretic dose (furosemide equivalents, mg)	40 (20, 80)	40 (20, 80)
Antiarrhythmic therapy	23% (123)	29% (146)
Amiodarone	19% (106)	24% (120)
Sotalol	2% (12)	4% (19)
Dofetilide	1% (4)	1% (3)
Mexiletine*	1% (3)	1% (3)
Moricizine	<1% (1)	<1% (1)
Procainamide	<1% (1)	0
QRS interval (ms)	120 (100, 160)	120 (100, 160)
Intraventricular conduction	(N = 533)	(N = 488)
Normal	26% (141)	23% (113)
LBBB	10% (51)	10% (51)
RBBB	3% (17)	4% (19)
IVCD	13% (70)	16% (76)
Paced	48% (254)	47% (229)
BiV pacing	41% (224)	42% (211)

Values are median (25th and 75th percentiles) or % (n). *4 patients on mexiletine regimen were also receiving another antiarrhythmic: 2 were taking amiodarone, 1 was taking sotalol, and 1 was taking procainamide.

ACE = angiotensin-converting enzyme; AF = atrial fibrillation; AFL = atrial flutter; ARB = angiotensin receptor blockade; BiV = biventricular; COPD = chronic obstructive pulmonary disease; CPX = cardiopulmonary exercise test; HF = heart failure; ICD = implantable cardioverter-defibrillator; IVCD = intraventricular conduction delay (nonspecific); KCCQ = Kansas City Cardiomyopathy Questionnaire; LBBB = left bundle branch block; LVEF = left ventricular ejection fraction; MDRD = Modification of Diet in Renal Disease; MI = myocardial infarction; NYHA = New York Heart Association; RBBB = right bundle branch block; VF = ventricular fibrillation; VT = ventricular tachycardia.

to the 3-month cardiopulmonary exercise test were compared between those with and without an ICD by using the Wilcoxon rank sum test.

SAS version 9.1 software (SAS Institute, Inc., Cary, North Carolina) was used for all analyses. We used a 2-tailed alpha level of 0.05 to test for all statistical significance.

Results

Patient characteristics. Among 2,331 HF-ACTION patients, 1,053 (45%) patients had an ICD at baseline. Baseline characteristics are shown in Table 1. The median age was 61 years old, 21% of patients were female, and 61% had ischemic cardiomyopathy; the median QRS duration was 120 ms, 41% received biventricular pacing, and 94% received beta-blocker agents. At enrollment, ICD patients randomized to exercise training (n = 546) and those to usual care (n = 507) were generally comparable in terms of their clinical characteristics.

ICD shocks and exercise therapy. Among those patients with an ICD at baseline who were randomized to exercise training, 65% (n = 357 of 546) completed 36 training sessions. The median total exercise time (25th, 75th percentiles) per week in the first 3 months was 81 (43, 199) min per week; 95 (24, 196) min per week in months 4 to 6; 77 (0, 184) min per week in months 10 to 12; and 54 (0, 157) min per week after 12 months.

Over a median 2.2 years of follow-up, 20% (108) of the exercise patients had a shock, compared to 22% (113) of the control patients. The median (25th, 75th percentiles) time to the first ICD shock was 11.4 (4.9, 19.0) months. We examined the factors associated with ICD shocks in unadjusted (single-predictor) Cox models (Table 2). Nonwhite race, lower systolic and diastolic blood pressure levels, abbreviated cardiopulmonary exercise test duration, higher slope of the increase of ventilation relative to Co_2 output,

Table 2 Unadjusted Factors Associated With the Occurrence of ICD Shocks

Variable	HR	95% CI	p Value
Age ≥60 yrs	0.98	0.93–1.03	0.44
Female	0.91	0.65–1.26	0.56
Nonwhite race	1.36	1.02–1.82	0.036
Previous MI	1.05	0.81–1.37	0.70
LVEF per 5% increase	1.03	0.93–1.13	0.58
Beck score ≥8	1.01	0.99–1.02	0.45
CCS angina class			
II–IV vs. none	1.25	0.81–1.94	0.68
I vs. none	1.18	0.73–1.89	
Diabetes	0.83	0.62–1.12	0.22
COPD	0.93	0.60–1.45	0.76
Smoking status			
Previous vs. never	1.14	0.84–1.55	0.42
Current vs. never	1.30	0.87–1.94	
Systolic BP per 10 mm Hg increase	0.92	0.85–0.99	0.03
Diastolic BP per 10 mm Hg increase	0.60	0.42–0.87	0.006
Resting HR per 5 beats/min increase	1.03	0.96–1.10	0.40
Body mass index per 1-U increase	1.01	0.98–1.03	0.60
Duration of CPX per 1-min increase	0.96	0.93–1.00	0.044
Peak Vo_2 per 1 ml/kg/min increase	0.98	0.95–1.01	0.21
$VeVCo_2$ slope per 5-U increase	1.42	1.05–1.92	0.022
Training heart rate per 5 beats/min increase	0.97	0.93–1.02	0.23
Exercise-induced dysrhythmia*	1.69	1.25–2.28	0.001
Previous AF/AFL	1.47	1.11–1.94	0.007
Previous sustained VT/VF	1.78	1.36–2.32	0.001
Biventricular pacing	0.93	0.71–1.22	0.60
Beta-blocker	0.67	0.42–1.09	0.11
Digoxin	1.36	1.04–1.78	0.024
ACE inhibitor/ARB	1.28	0.72–2.30	0.40
Statin	0.87	0.67–1.14	0.31
Aldosterone antagonism	1.08	0.83–1.41	0.57
Loop diuretic	1.23	0.76–1.99	0.40
Aspirin	1.13	0.85–1.49	0.40
Antiarrhythmic therapy	1.19	0.89–1.60	0.24

*Exercise-induced dysrhythmia was defined in the HF-ACTION cardiopulmonary exercise test protocol as any exercise test complicated by serious arrhythmia (supraventricular tachycardia, sustained ventricular tachycardia, or fibrillation ≥7 PVCs/min, ventricular bigeminy or trigeminy, or nonsustained ventricular tachycardia (≥3 beats).

BP = blood pressure; CCS = Canadian Cardiovascular Society; CI = confidence interval; HR = hazard ratio; PVC = premature ventricular contraction; $VeVCo_2$ = ventilation (VE) and carbon dioxide output (VCo_2) slope; other abbreviations are as in Table 1.

exercise-induced dysrhythmia, previous atrial fibrillation or flutter, previous sustained ventricular tachycardia or fibrillation, and digoxin pharmacotherapy were associated with the occurrence of ICD shocks.

Using Cox proportional hazards modeling, we identified independent predictors of ICD shocks. Figure 1 details those factors associated with the occurrence of ICD shocks after adjusting for prognostically important variables. Factors significantly associated with an increased risk of ICD shock were previous sustained ventricular tachycardia/ventricular fibrillation, atrial flutter or atrial fibrillation, lower diastolic blood pressure, exercise-induced dysrhythmia, and nonwhite race. After adjustment for the identified predictors of shock, exercise training was not associated with the occurrence of ICD shocks (hazard ratio [HR]: 0.90 [95% confidence interval (CI): 0.69 to 1.18], p = 0.45). Adjusted shock-free survival according to exercise therapy versus that in usual care is shown in Figure 2.

Sensitivity analysis. Consistent with the conduct of a trial of patients with HF, 29% (n = 376 of 1,278) of patients who did not have an ICD at baseline received an ICD in follow-up. In order to assess the impact of new ICD implants on the association of exercise training and ICD shocks, we conducted a sensitivity analysis in which all ICD patients were included (ICD at baseline or implanted during follow-up). Results of the primary model and the model including all ICD patients (at baseline and follow-up) were consistent (Table 3). There was no association between exercise therapy and ICD shocks.

Exercise training and additional clinical outcomes in ICD patients. The primary efficacy endpoint in the overall HF-ACTION trial was the composite endpoint of all-cause mortality and hospitalization. Hospitalization or death occurred in 67% (709 of 1,053) of those with ICDs at baseline versus 63% (809 of 1,278) in patients without an ICD at baseline. There were no differences in risk of hospitalization or death according to the presence of an ICD at baseline (HR: 0.99 [95% CI: 0.86 to 1.14], p = 0.90).

We also examined the occurrence of the combined endpoint of shock or death according to randomized therapy (exercise training versus control). Among 1,053 patients with ICDs at baseline, 353 (34%) patients met the composite shock/death endpoint, including 177 (35%) among 507 patients in the usual care group and 176 (32%) of 546 patients in the exercise training group. Exercise training was not associated with the combined endpoint of shock or all-cause mortality (HR: 0.94 [95% CI: 0.75 to 1.18], p = 0.58). Finally, changes in peak Vo_2 (baseline to 3 months) at cardiopulmonary exercise testing were not significantly different between those with and without an ICD (Table 4).

Outcomes following ICD shocks. Among the 1,053 patients with ICDs at baseline, 433 (41%) patients experienced the composite endpoint of death, myocardial infarction, or worsening HF, including 66 (40%) of 163 patients with a shock and 367 (41%) of 890 patients without a shock. The occurrence of shock was marginally associated with the composite endpoint of death, myocardial infarction, or worsening HF (HR: 1.39 [95% CI: 0.99 to 1.94], p = 0.053).

Discussion

There are 2 major findings from this analysis of exercise training in patients with HF and ICDs. First, consistent with our primary hypothesis, exercise therapy is not associated with an increase in all-cause ICD shocks. Second, ventricular arrhythmias induced during exercise testing are associated with ICD shocks; therefore, exercise testing may be useful in ICD patients before beginning a structured exercise program.

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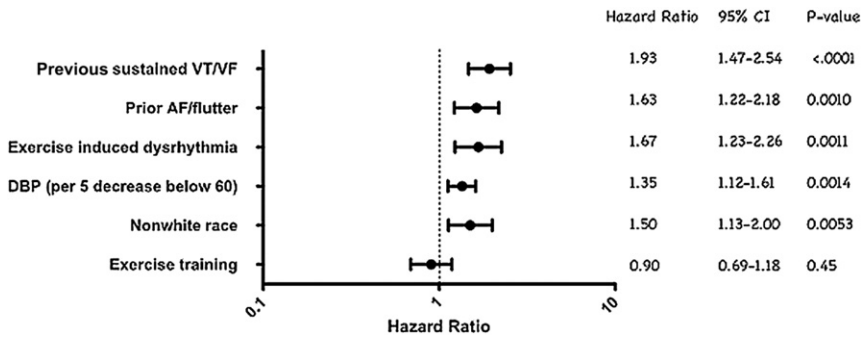

Figure 1 **Multivariable Predictors of ICD Shocks in Patients With Symptomatic HF and LVEF ≤35%**

The forest plot shows hazard ratios for the occurrence of implantable cardioverter-defibrillator (ICD) shocks after accounting for other prognostic factors. Exercise training was not associated with an increased hazard of shock (p = 0.45). Exercise-induced dysrhythmia was defined as a cardiopulmonary exercise test (CPX) stopped because of serious arrhythmia or because frequent ventricular ectopy occurred, either during CPX test or during recovery. AF = atrial fibrillation; CI = confidence interval; DBP = diastolic blood pressure; HF = heart failure; LVEF = left ventricular ejection fraction; VT/VF = ventricular tachycardia/ventricular fibrillation.

Exercise therapy maximizes cardiopulmonary reserve and functional status in patients with HF (18). However, exercise increases heart rate and adrenergic tone and may lead to arrhythmias. Guidelines advocate exercise training to improve clinical status in ambulatory patients with current or previous symptoms of HF and reduced LVEF (Class I; Level of Evidence: B) (10). Despite the frequency of ICD implantation and guideline recommendations encouraging exercise training, few prospective data are available regarding the safety of exercise therapy in HF patients with ICDs. Available data suggest that physicians and patients have various opinions regarding exercise and sports participation in ICD populations (19).

Initial studies of exercise and ventricular arrhythmias concentrated on the diagnostic aspects of exercise testing in patients with known arrhythmias. Allen et al. (6) analyzed the results of exercise testing in 64 patients with documented ventricular tachycardia or fibrillation with or without HF. Use of the Bruce protocol or low-level exercise could reproduce ventricular arrhythmias in 42% of subjects (34% nonsustained and 8% sustained) (6). There were no adverse events or major complications. The investigators concluded that exercise testing was safe and could be used to provoke ventricular arrhythmias. Subsequent studies have evaluated the safety of exercise testing in HF patients with and without previous arrhythmias. Keteyian et al. (20) analyzed the safety of symptom-limited peak cardiopulmonary stress testing in patients with symptomatic HF. During a total of 4,411 peak-exercise tests in HF-ACTION, there was 1 episode of ventricular fibrillation, 1 episode of sustained ventricular tachycardia, and no procedure-related deaths (20).

Recently, an international registry of young ICD patients (mean LVEF of 60%) demonstrated that 9% of athletes receive a shock during competitive sports (21). Fewer data are available regarding the safety of exercise in patients with HF and ICDs. Single-center experiences with small cohorts of ICD patients have demonstrated the feasibility of cardiopulmonary rehabilitation programs without evidence of major safety concerns (12,22,23). One of the larger series

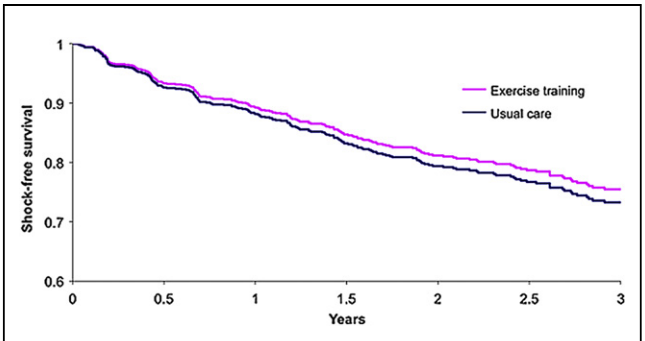

Figure 2 **Adjusted (Predicted) Shock-Free Survival in Patients With ICDs at Baseline in the HF-ACTION Trial According to Randomized Treatment (Exercise Training Plus Usual Care vs. Usual Care Alone)**

After adjustment for the identified predictors of shock, exercise training was not associated with the occurrence of implantable cardioverter-defibrillator (ICD) shocks (hazard ratio: 0.90 [95% confidence interval: 0.69 to 1.18], p = 0.45). The adjusted (predicted) shock-free survival according to exercise therapy versus usual care is shown.

Table 3 **Results of Sensitivity Analysis Including All Patients With an ICD**

Variable	Baseline ICD Patients	All ICD patients
Previous sustained VT/VF	1.93 (1.47–2.54)	1.90 (1.49–2.41)
Previous AF/AFL	1.63 (1.22–2.18)	1.72 (1.35–2.20)
Exercise-induced dysrhythmia	1.67 (1.23–2.26)	1.53 (1.17–2.00)
Diastolic blood pressure (per 5 mm Hg below 60)	1.35 (1.12–1.61)	1.25 (1.06–1.47)
Nonwhite race	1.50 (1.13–2.00)	1.53 (1.20–1.94)
Exercise training	0.90 (0.69–1.18)	0.96 (0.76–1.21)

Values are HR (95% CI).
Abbreviations as in Tables 1 and 2.

Table 4 Changes in Peak Vo_2 (ml/kg/min) From Baseline to 3 Months According to ICD Status at Baseline

Variable	ICD*	No ICD	Wilcoxon Rank Sum p Value
All patients			
n	852	978	
Mean (SEM)	0.42 (0.08)	0.62 (0.08)	0.067
Median (25th, 75th percentiles)	0.3 (−1.0, 1.7)	0.5 (−0.9, 2.0)	
Exercise training			
n	452	502	
Mean (SEM)	0.69 (0.12)	0.91 (0.11)	0.085
Median (25th, 75th percentiles)	0.4 (−0.8, 2.1)	0.9 (−0.7, 2.4)	
Usual care			
n	400	476	
Mean (SEM)	0.11 (0.12)	0.31 (0.12)	0.35
Median (25th, 75th percentiles)	0.1 (−1.2, 1.4)	0.2 (−1.1, 1.4)	

*Patients who received an ICD after baseline are included in the "No ICD" group if the implantation did not occur until after the 3-month CPX test. Patients missing peak oxygen consumption change data (n = 201 ICD patients and n = 261 patients without ICD) and patients who received an ICD between baseline and the 3-month CPX test (n = 39) were omitted.

Abbreviations as in Table 1.

compared exercise training between 92 patients with an ICD and 473 patients without an ICD (11). Following 3 months of training (3 times/week), the ICD group experienced a total of 13 shocks: 5 appropriate shocks during training, 7 appropriate shocks in between sessions, and 1 inappropriate shock during training. The ICD group experienced an improvement in Vo_2, but the improvement was less pronounced than in the non-ICD patients. Based upon these results, the investigators concluded that exercise-training is safe in ICD patients and leads to favorable results. However, given the small amount of time spent exercising relative to that of nonexercise, the ICD patients did have an increased shock frequency during the exercise versus nonexercise periods (6 vs. 7, respectively).

HF-ACTION afforded the opportunity to examine the safety of exercise training among patients with ICDs in the setting of a randomized trial and to assess the safety of exercise therapy in long-term follow-up. Over 2.2 median years of follow-up, 1 in 5 patients randomized to exercise therapy experienced an ICD shock. However, in both unadjusted and adjusted (adjusted HR: 0.90 [95% CI: 0.69 to 1.18, p = 0.45) settings, there were no differences in risk of ICD shocks or composite endpoint of ICD shocks or death between those randomized to exercise training and those who were randomized to usual care alone. Additionally, there were no differences in peak Vo_2 improvements between those with and without ICDs. These results provide reassurance that exercise training in HF patients with an ICD does not lead to an increased incidence of symptomatic ICD therapy. Finally, and perhaps more importantly, our data also suggest that the improvements in cardiopulmonary capacity are preserved in patients with ICDs.

It is important to note that, within HF-ACTION, the lower limit for tachycardia detection was programmed above the peak heart rate achieved on exercise testing. Although our data cannot exclude the possibility that there may have been differential rates of antitachycardia pacing (ATP) or cause-specific shocks, it would be unlikely for differences in appropriate and inappropriate therapies to be balanced across both arms such that there would be no overall difference. Additionally, as ATP is not uniformly effective, one would not expect ATP to be increased in the exercise arm without a corresponding increase in total shock burden.

Predictors of ICD shocks identified in HF-ACTION may be helpful when evaluating a given patient's candidacy for exercise training. Patients who had evidence of exercise-induced dysrhythmia did have a 67% higher risk of ICD shocks. Therefore, diagnostic exercise testing may be useful when evaluating patients with an ICD before recommending exercise training. Additionally, based upon the study protocol, the peak heart rate achieved during exercise testing is likely to be informative when programming the patient's ICD to maximize avoidance of inappropriate shocks. Consistent with the findings of large ICD trials, both previous atrial arrhythmias and ventricular arrhythmias were associated with an increased risk of shocks (16). This highlights the importance of optimizing beta-blockade in these patients.

Study limitations. There are several limitations to consider when evaluating the results. First, HF-ACTION was a randomized controlled trial of exercise and therefore represents a select population of HF patients. Second, our data are subject to the usual limitations inherent in post hoc analyses of prospective randomized data. Tempering this limitation is the fact that ICD therapy was a prospectively collected adverse event. Sites were educated and instructed to capture ICD therapy cases, a relatively common event in the care of HF patients. We did not have centralized adjudication of ICD events; therefore, appropriate and inappropriate ICD therapies could not be distinguished in this study. Although both are associated with adverse outcomes, they are fundamentally different.

HF-ACTION enrolled a heterogeneous population of ICD patients who likely had wide differences in device programming and therapies, factors known to influence the frequency of ICD shocks. However, the diversity of the ICD population also enhances the generalizability of these results. It is also important to note that the trial was unblinded and that knowledge of treatment group could have affected reporting of shocks and other outcomes. Finally, lower limits for tachyarrhythmia detection were reviewed and reprogrammed when indicated in HF ACTION. This practice may not be uniform in clinical practice and could lead to inappropriate shocks.

Conclusions

We found no evidence of increased ICD shocks in patients with HF and LV dysfunction who underwent exercise

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training. Exercise therapy should not be prohibited in ICD recipients with HF for fear of inducing ventricular dysrhythmias that precipitate ICD firing. Exercise testing may be helpful in screening patients at increased risk for exercise-associated shocks.

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