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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