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Addition of Supervised Exercise Training to a Post-Hospital Disease Management Program for Patients Recently Hospitalized With Acute Heart Failure

The EJECTION-HF Randomized Phase 4 Trial

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ABSTRACT

OBJECTIVES This study sought to measure the impact on all-cause death or readmission of adding center-based exercise training (ET) to disease management programs for patients with a recent acute heart failure (HF) hospitalization.

BACKGROUND ET is recommended for patients with HF, but evidence is based mainly on ET as a single intervention in stable outpatients.

METHODS A randomized, controlled trial with blinded outcome assessor, enrolling adult participants with HF discharged from 5 hospitals in Queensland, Australia. All participants received HF-disease management program plus supported home exercise program; intervention participants were offered 24 weeks of supervised center-based ET. Primary outcome was all-cause 12-month death or readmission. Pre-planned subgroups included age (<70 years vs. older), sex, left ventricular ejection fraction (≤40% vs. >40%), and exercise adherence.

RESULTS Between May 2008 and July 2013, 278 participants (140 intervention, 138 control) were enrolled: 98 (35.3%) age ≥70 years, 71 (25.5%) females, and 62 (23.3%) with a left ventricular ejection fraction of >40%. There were no adverse events associated with ET. There was no difference in primary outcome between groups (84 of 140 [60.0%] intervention vs. 90 of 138 [65.2%] control; p = 0.37), but a trend toward greater benefit in participants age <70 years (OR: 0.56 [95% CI: 0.30 to 1.02] vs. OR: 1.56 [95% CI: 0.67 to 3.64]; p for interaction = 0.05). Participants who exercised to guidelines (72 of 101 control and 92 of 117 intervention at 3 months) had a significantly lower rate of death and readmission (91 of 164 [55.5%] vs. 41 of 54 [75.9%]; p = 0.008).

CONCLUSIONS Supervised center-based ET was a safe, feasible addition to disease management programs with supported home exercise in patients recently hospitalized with acute HF, but did not reduce combined end-point of death or readmission. (A supervised exercise programme following hospitalisation for heart failure: does it add to disease management?; ACTRN12608000263392) (J Am Coll Cardiol HF 2018;6:143–52) © 2018 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

ET = exercise training

HF = heart failure

HF-DMP = heart failure disease management program

HFpEF = heart failure with preserved ejection fraction

IQR = interquartile range

OR = odds ratio

Exercise training (ET) has physiological and clinical outcome benefits in stable outpatients with heart failure (HF), with improved exercise tolerance, improved quality of life, and reduced HF-related and all-cause readmissions (1). Current guidelines recommend that patients with HF should be encouraged to undertake regular aerobic exercise (2,3), including referral to supervised ET programs (4). However, there are gaps in the evidence (1,5). Trials have enrolled patients with chronic HF stabilized on optimal medical therapy, so that the feasibility, safety, and effectiveness of ET in the early post-hospital setting remain unclear (6). ET has largely been tested as a single intervention, despite evidence that coordinated multidisciplinary HF disease management programs (HF-DMPs) reduce mortality and readmissions in recently hospitalized patients with HF (2,7). HF-DMPs offer an opportunity to provide supported home exercise advice, and may also provide an efficient setting for center-based ET (8). Limited trials have examined ET in the setting of HF-DMP (9–11), and whether ET has an additive effect to HF-DMPs is unclear. Supported home ET may have similar benefits to supervised center-based ET (12), but no trial has compared the addition of center-based ET to a supported home exercise program. Women (13), older patients (14), and patients with heart failure with preserved ejection fraction (HFpEF) (15,16) remain underrepresented in ET trials. Access to center-based ET remains limited (17), and exercise adherence is a challenge in real-world practice (18).

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The aim of this pragmatic, multicenter, randomized, controlled trial was to investigate the feasibility, safety, and effectiveness of delivering supervised center-based ET as part of a HF-DMP for recently hospitalized patients with HF compared with HF-DMP alone. In recognition of current guidelines, HF-DMP included a supported home exercise program. Our primary hypothesis was that participants allocated to supervised center-based ET plus HF-DMP would have a reduction in the composite outcome of all-cause death and hospitalization over 12 months compared with HF-DMP. We also aimed to explore the benefits in women, older participants, and participants with HFpEF, and measure the impact of the combined intervention on exercise outcomes and quality of life.

METHODS

STUDY DESIGN. The EJECTION-HF (Exercise Joins Education: Combined Therapy to Improve Outcomes in Newly-discharged Heart Failure) was a multicenter randomized controlled trial conducted in 5 hospitals in Queensland, Australia, which each had an established HF-DMP (19). Human research ethics approval was obtained from all sites, with central coordination by the Royal Brisbane and Women's Hospital Human Research Ethics Committee.

PARTICIPANTS. Adult hospital inpatients with HF as a major contributing diagnosis were identified by HF-DMP staff and screened for eligibility by a research officer. Detailed inclusion and exclusion criteria have been reported previously (19); in brief, potential participants were willing and able to attend a 12-week HF-DMP, and assessed as suitable for supervised moderate intensity ET. All participants provided written informed consent.

RANDOMIZATION AND MASKING. Participants were randomized to control (HF-DMP with supported home exercise program), or intervention (HF-DMP with supported home exercise program plus supervised center-based ET). Allocation was undertaken by the project manager, after obtaining consent and baseline assessment by the research officer. Allocation was based on computerized random sequence generation by the statistician in blocks of 10, stratified by site, provided in sealed opaque envelopes to the project manager. The project manager notified the HF-DMP of participant allocation and helped to coordinate their program commencement, and was responsible for data management, but not program delivery or data collection. Participants and HF-DMP staff were aware of their treatment group. Clinical outcomes were collected by a single trained research officer masked to group assignment.

PROCEDURES. HF-DMP (all participants). All sites offered a multidisciplinary HF-DMP including active in-hospital case finding, clinic visits, and telephone support to provide education, symptom monitoring, medication titration, and social support. The HF-DMP included 12 weeks of weekly review with disease monitoring, review and progression of the home exercise program, and weekly structured self-management education classes (HF pathophysiology, symptom monitoring, medications, dietary advice, stress management, risk factor modification, and exercise advice). The HF-DMP was delivered with a rolling start to support timely commencement. Each HF-DMP had access to a cardiologist, HF trained nursing staff, pharmacist, and exercise professional (physiotherapist and/or exercise physiologist), although programs were adapted to local resourcing. Two investigators (senior exercise professionals in one HF-DMP) developed the exercise protocols and