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Impact of Exercise Programs on Hospital Readmission Following Hospitalization for Heart Failure: A Systematic Review

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Abstract

Given persistently high 30-day readmission rates among patients hospitalized for heart failure, there is an ongoing need to identify new interventions to reduce readmissions. Although exercise programs can improve outcomes among ambulatory heart failure patients, it is not clear whether this benefit extends to reducing readmissions following heart failure hospitalization. We therefore conducted a systematic review of the literature to identify randomized controlled trials examining the impact of exercise programs on hospital readmissions among patients recently hospitalized for heart failure. We searched Ovid MEDLINE, EMBASE, and the Wiley Cochrane Library for studies that fulfilled pre-defined criteria, including that the exercise program pre-specify activity type and exercise frequency, duration, and intensity. Exercise interventions could occur at any location including within the hospital, at an outpatient facility, or at home. Among 1213 unique publications identified, only one study fulfilled inclusion criteria. This study was a single-site randomized controlled trial that consisted of a 12-week exercise program in a cohort of 105 patients with a principal diagnosis of HF at a metropolitan hospital in Australia. This study revealed a reduction in 12-month all-cause and cardiovascular-related hospitalization rates.

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Compliance with Ethics Guidelines

Human and Animal Rights and Informed Consent

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study formal consent is not required.

Conflict of Interest

Drs Goyal and Delgado declare no conflict of interests

However, inferences were limited by its single-site study design, small sample size, premature termination, and high risk for selection, performance, and detection bias. As no studies have built upon the findings of this study, it remains unknown whether exercise programs can improve readmission rates among patients recently hospitalized for heart failure, a significant gap in the literature.

Keywords

Heart Failure; Readmission; Randomized Controlled Trials

INTRODUCTION

The prevention of readmissions among older adults hospitalized for heart failure (HF) has been an increasing focus of federal policy and clinical practice. Hospital 30-day readmission rates for HF are publicly reported on the Medicare Hospital Compare website [1] and are used to direct financial penalties toward hospitals with higher-than-expected readmission rates after case-mix adjustment [2]. As a result, hospitals across the United States have implemented new strategies designed to improve both hospital and transitional care for patients with HF [3].

One challenge with readmission reduction in HF is that few strategies have demonstrated consistent benefits, underscoring the ongoing need to identify new interventions to further reduce readmissions. According to a recent systematic review, intensive home visit strategies can reduce readmissions within 30 days of discharge[4]. However, other tested interventions including multi-disciplinary HF clinics, telemonitoring, and educational strategies were not consistently associated with lower short-term readmissions. Notably, the impact of exercise-based interventions on readmissions was not explicitly addressed in this review, nor has it been addressed by any other systematic reviews to date.

Given their many cardiovascular benefits [5–8], exercise programs may offer a particularly promising strategy to reduce readmissions. Exercise is a form of physical activity that is structured and repetitive over an extended period of time, with the intention of improving fitness, performance or health [9]. Exercise programs which specify activity type, frequency, duration, and intensity have been shown to improve outcomes among HF patients through increased health-related quality of life [10–17] and reduced rates of hospitalization for all causes [10, 13, 17] and HF in particular [10, 18, 17]. Although these programs appear safe even among patients with recently decompensated HF [19], it is uncertain what the role of exercise programs should be among recently hospitalized patients to reduce both all-cause and HF-related readmissions.

Accordingly, we conducted a systematic review of the literature to identify randomized controlled trials (RCT) examining the impact of exercise programs on readmissions to the hospital following hospitalization for HF.

METHODS

Data Sources and Searches

We searched Ovid MEDLINE, EMBASE, and the Wiley Cochrane Library (CENTRAL) for human-only studies published between database inception and April 7, 2016. We worked with an experienced research librarian (DD) to design a search strategy that would provide maximal sensitivity for identifying relevant RCTs. This strategy included use of the BMJ Clinical Evidence RCT search strategy filter [20]. Detailed specifications for the search methodology are provided in the online supplement (Online Resource 1).

Study Selection

We included English-language studies that examined the benefits of an exercise program for adults aged 18 years or older that was initiated either during or after a hospitalization for a principal diagnosis of HF. To capture the largest possible number of studies, we did not require that study enrollment occur within a specific time interval after hospitalization.

We required that exercise programs pre-specify activity type (which could be aerobic and/or resistance training), exercise frequency, exercise duration, and exercise intensity. Exercise could occur at any location including within the hospital, at an outpatient facility, or at home. The protocol could be tailored to an individual's baseline functional status and could involve changes in exercise frequency, duration, and/or intensity over the study period if done according to a pre-specified protocol.

We excluded interventions based on motivational interviewing, counseling, goal-setting, and/or education that did not incorporate a formal exercise program. We intended to assess the impact of the exercise itself rather than strategies primarily aimed at improving adherence to exercise. Although interventions to improve exercise adherence have yielded modest improvements in the uptake of exercise including cardiac rehabilitation [21–23], they have failed to demonstrate significant improvements in clinical outcomes such as hospital readmission rates [24–26]. Furthermore, such interventions have often been poorly characterized within the literature, thereby making their generalizability and application to typical clinical practice difficult.

We also excluded studies that did not report rates of hospital readmissions during the follow-up period. Readmissions could be for any diagnosis or for HF only and were permitted to occur up to one year following hospital discharge.

Data Extraction and Analysis

We selected and analyzed studies for inclusion according to the process outlined by the Cochrane handbook [27]. One team member (PG) reviewed all abstracts and titles to identify studies that were potentially eligible for inclusion and rejected those that were clearly ineligible. We then reviewed full-text articles to identify those for inclusion. A second team member (KD) independently reviewed a random sample of 20 records to ensure appropriate study screening and selection. Agreement between team members was complete (kappa 1.0). To maximize the sensitivity of our literature search, we additionally reviewed related articles

identified in a recent Cochrane review on exercise-based rehabilitation for HF [17]. Using Scopus, we used reverse citation indices to identify and screen additional articles for eligibility.

We constructed summary tables for included articles describing sample size, setting and study population, inclusion/exclusion criteria, baseline subject characteristics, intervention and comparison group studied, outcome metrics and readmission-related results, follow-up period, and judgments for the risk-of-bias. Two team members (PG and KD) independently performed a risk-of-bias assessment for each included article using the Cochrane Effective Practice and Organization Care (EPOC) Groups' Risk of Bias criteria [28], which describes bias related to randomization, blinding, selective reporting, and attrition. Kappa was 1.0, indicating no disagreement.

RESULTS

Selection of Studies

Our search yielded 1942 records, of which 1213 represented unique publications (Figure 1). After reviewing all titles and abstracts, we identified 80 potentially eligible studies that broadly examined exercise in populations with HF. Excluded studies predominantly examined pharmacologic or device-based therapies for HF, or patients recently hospitalized with acute myocardial infarction.

Among the 80 potentially-eligible studies, 26 were conference abstracts, 12 were meta-analyses, 8 described the methods of an ongoing or future trial, and 4 were unavailable in English. We subsequently excluded these 50 records. We reviewed the full-texts for the remaining 30 records, yielding one study that fulfilled our pre-specified criteria of examining the impact of an exercise program on the rate of readmission in a population recently hospitalized for HF. We reviewed an additional 128 records identified from the 2014 Cochrane review on exercise rehabilitation [17] and Scopus, yielding no additional studies for inclusion. Figure 1 reveals a PRISMA flow diagram of records assessed with reasons for exclusion.

Description of the Included Study

The one study that fit our inclusion criteria was a single-site RCT, consisting of 105 patients [29]. Subjects were predominantly older adults, with a mean age of about 72 years, who were enrolled following an admission for a principal diagnosis of HF at a metropolitan hospital in Sydney, Australia (Table 1). The intervention included a 12-week exercise program individualized according to a baseline physical assessment. Each exercise session was comprised of a warm-up phase, a 30-minute exercise phase including both aerobic and resistance training, and a cool-down phase. Sessions were designed to occur at home, as well as once per week at a gymnasium with other enrollees. Subjects in the intervention group were also evaluated weekly by a clinical nurse consultant who could initiate treatment and/or refer patients to a medical practitioner for signs of decompensated HF. The control group received usual medical care. The primary endpoints were all-cause and cardiovascular-specific hospital readmission at 12 months after enrollment. Secondary endpoints included

mortality, the Minnesota Living with Heart Failure Questionnaire, the Heart Failure Needs Assessment Questionnaire, and the 6-minute walk test.

Although the results of this study revealed a reduction in 12-month all-cause and cardiovascular-related hospitalization rates, we noted several potential limitations. The study was small involving only 105 patients and was performed at a single-site in Australia. Although described as occurring post-hospitalization, the timing of the intervention in relation to hospital discharge was not reported, limiting inferences with regard to the appropriate timing of post-discharge exercise interventions. In addition, the study was prematurely terminated in 2001 prior to completion of targeted enrollment due to new nationwide mandates related to disease-management in Australia that made control group participation unethical. As a result, approximately one-half of the targeted sample size was achieved.

We also noted several sources of possible bias (Table 2). First, neither the participants nor the investigators were blinded to the assigned groups (intervention or control) at allocation or during outcome assessment, yielding high risk for performance and detection bias. Baseline characteristics were also notably different between groups with regard to the use of guideline-based medical therapy for HF at the time of study enrollment. For example, spironolactone use was 17% in the intervention arm and 2% in the control arm.

Description of Excluded Studies

Among the 29 full-text studies reviewed and excluded, 24 did not study a population recently hospitalized for HF, and 14 did not report hospital readmission rates as an outcome.

Three studies met multiple criteria for inclusion but were excluded for failing to meet significant study parameters. Austin et al [13] and Zwisler et al [30] conducted RCTs on the impact of a cardiac rehabilitation program on hospital readmissions among other outcomes. Although Austin et al studied patients with HF, only 25% (n=51) of the study cohort had been recently hospitalized. In addition, it was not known whether these hospitalizations were for heart failure. Although Zwisler et al exclusively studied recently hospitalized patients, only 12% (n=92) were for a principal diagnosis of HF. We therefore did not include either study, as readmission outcomes for those recently hospitalized for HF were not separately reported in either case, thereby precluding assessment of the impact of the exercise program on readmission reduction after HF hospitalization. In contrast, Smolis-Bak et al conducted an RCT on the impact of an exercise program with adjunctive home telemonitoring on exercise capacity and echocardiographic parameters among patients with HF who underwent implantation of a cardiac resynchronization therapy device during hospitalization [31]. Although they also reported readmission rates, we excluded this study because it was unclear whether patients had been hospitalized for acute decompensated HF or electively for the implantation procedure alone.

DISCUSSION

Our systematic review identified only one small single-center study examining the impact of an exercise program on readmission after hospitalization for HF. This finding demonstrates a

large gap in our understanding of the role of exercise in reducing patients' vulnerability to major adverse outcomes including readmission after hospital discharge. As exercise has been shown to provide both cardiovascular and non-cardiovascular benefits for patients with HF [32], our findings suggest that the examination of exercise in HF be extended to include recently hospitalized patients.

The benefits of exercise in patients with HF are well-documented. In a recent Cochrane review of 33 RCTs including 4740 subjects with HF, exercise-based rehabilitation reduced the risk of all-cause and HF-related hospitalization and improved health-related quality of life [17]. Although the majority of patients from that review had HF with reduced ejection fraction, there is a growing body of literature that suggests that exercise also improves outcomes in HF with preserved ejection fraction through improvements in health-related quality of life [33, 34] and exercise capacity [34–38]. These benefits have been achieved with relatively few side effects [34].

Whether the benefits of exercise programs extend to reducing readmissions after hospitalization for HF is unclear. The majority of studies investigating the impact of exercise programs on hospitalization in HF have involved stable ambulatory patients [17]. Consistent with this finding, our systematic review identified just one study that examined recently hospitalized patients [29] that was limited by its single-site study design, small sample size, premature termination, and high risk for selection, performance, and detection bias. This study was also performed more than 10 years ago, prior to the contemporary focus on readmission as a quality metric for hospitals. Since this time, no additional work has extended these results. Our extensive search for relevant studies led to our review of over 1200 unique publications. Although three studies almost fulfilled inclusion criteria, we intentionally excluded them because they did not report results for our primary population of interest—patients recently hospitalized with HF. Consequently, we still know very little about how exercise can improve post-hospital outcomes in a population that experiences a high rate of adverse events following hospital discharge [39–41], including a readmission rate approaching 25%.

The gap in evidence relating exercise to readmission after HF hospitalization has a number of potential explanations. It may be that providers view exercise as unsafe in patients hospitalized with HF, especially given the frequency of advanced age observed in this population [42], almost all of whom have multiple chronic conditions [43] including frailty [44]. However, exercise performed at home [45] and at rehabilitation facilities [19] has been shown to be safe, even among older persons [46, 47] with frailty [48], and is unlikely to cause many of the adverse events associated with medication use in heart failure such as electrolyte disorders, dehydration, fatigue, and reduced activity level [49]. It may also be that providers do not view behavioral and lifestyle interventions like exercise with the same enthusiasm as medications or device-based therapies. Yet exercise is a class I indication with level of evidence A in HF [42] and may be as effective as pharmacologic therapies used for heart failure, with less side effects [50]. Providers may in addition be reluctant to add an exercise regimen to an already-busy post-discharge period during which the patient is transitioning back home. However, initiating exercise programs soon after discharge can

improve downstream exercise rates [51], suggesting that the early-discharge period is not only appropriate, but may be an ideal period to test the effect of exercise interventions in HF.

The findings of our systematic review highlight a number of areas for further investigation. It is evident that additional studies are needed to evaluate whether exercise programs can reduce readmissions after HF hospitalization. As part of these studies, attention should be paid to understanding the optimal time period for initiating exercise programs in relation to a hospitalization. Currently, cardiac rehabilitation for HF is not reimbursable by Medicare until 6 weeks after hospital discharge [52] and therefore overlooks a particularly vulnerable period for many patients [41]. Given the stress encountered during the hospitalization itself and its potential link to further debilitation [53], some have suggested initiating exercise programs during the index hospitalization, an approach that will be addressed by the ongoing REHAB-HF study[54]. While REHAB-HF is not powered to detect differences in readmissions, this study should aid in the design of future research addressing this outcome. Although the benefits of exercise appear to be independent of type, dose, or setting [17, 55], the exact approach will likely need to be tailored to the unique capacities and vulnerabilities of recently discharged patients, which likely differ from those of ambulatory patients. Where appropriate, new technologies like actigraphy in the form of wrist-worn accelerometers also warrant study, as they may be able to facilitate individualized home-based exercise programs and increase adherence [56].

Study Limitations

There are some important limitations to our systematic review. It is possible that we did not include all relevant studies in this review, as we screened select databases and only included studies available in the English language. However, we worked with an experienced research librarian and searched multiple databases screening 1213 records for relevant studies. Also, we did not include exercise-based interventions whose type, frequency, intensity, and duration were not pre-specified. We believe that without adequate characterization, assessment and dissemination of the exercise intervention would be limited.

CONCLUSION

We found inadequate data on the role of exercise programs to reduce readmissions among patients recently hospitalized for HF, highlighting a major knowledge gap. At a time when readmission rates remain high despite a decade of ongoing research and efforts to reduce them through improved hospital and transitional care, there is a need to identify new strategies to further improve patient outcomes. Exercise programs offer one promising avenue that warrants further investigation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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- Of importance
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Figure 1.
PRISMA Flow Diagram

Table 1

Characteristics of the Included Study

Davidson et al 2010	
<i><u>Characteristic</u></i>	<i><u>Details</u></i>
Sample Size:	N=105 (Intervention 53, Control 52)
Setting:	Sydney, Australia; Single-Center
Study Population:	Recently hospitalized for a primary diagnosis of HF
Inclusion Criteria:	Any age; any etiology of HF; NYHA Class I-IV; cleared by their physician to participate in an exercise program
Exclusion Criteria:	Unstable angina pectoris
Baseline Characteristics:	<u>Intervention</u> : 71.6 years, 64% Male, NYHA II/III 38%/60% <u>Control</u> : 73.9 years, 60% Male, NYHA II/III 33%/67% Race, HF Etiology, LVEF not reported.
Intervention:	12-week structured exercise program individualized according to a baseline physical assessment; weekly visit with a clinical nurse consultant
Comparison:	Usual medical care
Outcome Measures:	<u>Primary endpoints</u> : All-cause and cardiovascular-specific hospital readmission. <u>Secondary endpoints</u> : Mortality, the Minnesota Living with Heart Failure Questionnaire, the Heart Failure Needs Assessment Questionnaire, and the 6-minute walk
Readmission-related Results:	All-cause readmission rate: Intervention 44% vs. Control 69%, p<0.01; Cardiovascular-specific readmission rate: Intervention 24% vs. Control 55%, p=0.001
Follow-up Period:	12 months

Abbreviations: NYHA New York Heart Association; HF Heart Failure; LVEF Left ventricular ejection fraction

Table 2

Risk-of-Bias of the Included Study

Davidson et al 2010	
<i>Characteristic</i>	<i>Details</i>
Random sequence generation: (Selection bias)	<u>Low Risk</u> . "Participants were randomized to either the intervention or control group by means of a computer-generated program"
Allocation concealment: (Selection Bias)	<u>Low Risk</u> . "The randomization technique was blinded to the investigators until the close of the study"
Blinding: (Performance bias and Detection bias)	<u>High risk</u> . Neither the participants nor investigators were blinded to the interventions at allocation or during outcome assessment
Selective reporting: (Reporting bias)	<u>Low Risk</u> . "All pre-selected outcome metrics were reported"
Intention-to-treat analysis?	<u>Low Risk</u> . "All analyses were carried out on an intention-to-treat basis"
Incomplete outcome data?	<u>Low Risk</u> . "No participants were lost to follow-up"
Group balanced at baseline?	<u>High risk</u> . "Significantly greater proportion of people in the intervention group were taking spironolactone at baseline"
Groups received same intervention?	<u>Low risk</u> . The groups were treated in a similar fashion apart from the intervention