Impact of exercise training program attendance and physical activity participation on six minute walk distance in patients with heart failure

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Exercise training is recommended for all people with stable heart failure (HF) (Sagar et al, 2015). Despite well documented benefits, adherence to this intervention by people with HF is poor (Conraads et al, 2012; Piepoli et al, 2015). Structured, center-based exercise training programs remain the cornerstone of current exercise recommendations, however poor attendance and high drop out rates are common, both of which compromise short and long term outcomes (Conraads et al, 2012; Hammill, Curtis, Schulman, and Whellan, 2010; van der Wal et al, 2010). Adherence to physical activity guidelines is poor in people with HF (Klompstra, Jaarsma, and Stromberg, 2015) and failure to meet these guidelines is associated with poorer clinical outcomes (Doukky et al, 2016). Physical activity incorporates structured exercise training as well as all recreational, occupational and functional activities undertaken by an individual. Current guidelines recommend that individuals undertake 150-300 minutes of moderate intensity activity or 75 - 150 minutes of vigorous intensity activity per week (Eckel et al, 2014) or a combination of both.

Surprisingly little is known about the exercise behaviours of people with HF, and in particular, those recently hospitalized. Many exercise training trials have been conducted in stable and select populations and exercise program adherence is often poorly reported (Deka, Pozehl, Williams, and Yates, 2017). Physical activity undertaken outside of health facilities, and change in physical activity associated with an intervention, are also rarely described. Several studies have previously sought to identify predictors of exercise behaviour in people with HF. Very few studies however, have specifically investigated the impact of program attendance and physical activity participation, and the inter-relationship between these variables, on change in exercise capacity. Understanding these variables in more detail may assist clinicians
to deliver exercise training programs specifically targeted for best effect, thereby assisting individuals to make meaningful and sustainable change.

The aim of the current study was to describe patterns of exercise training program attendance and physical activity participation in a sample of recently hospitalized patients enrolled in a comprehensive HF disease management program. An additional aim was to measure the association between program attendance (frequency and duration of attendance) and physical activity participation with change in six minute walk distance (6MWD). We hypothesised that program attendance variables and physical activity participation would be independently associated with improvements in 6MWD at 12 weeks.

Methods

Study design and participants

This study is a secondary analysis of the EJECTION-HF trial (ACTRN12608000263392). The design and primary outcomes of the EJECTION-HF trial, as well as detailed inclusion and exclusion criteria, have been reported previously (Mudge et al, 2018; Mudge et al, 2011). In brief, this multi-center, randomized controlled trial evaluated outcomes from a center-based exercise training program, delivered as a component of a comprehensive disease management program for patients recently (within six weeks) hospitalized with HF. Participants were recruited from HF services at three major metropolitan hospitals and two community facilities in south east Queensland, Australia, from 2008-2013. This secondary analysis is confined to participants in the intervention group only, who were randomized to receive the center-based exercise training program. Informed consent was obtained from all participants. The study complied with the Declaration of Helsinki and was approved by the Human Research Ethics
Committee (HREC) at each participating site, centrally co-ordinated by the Royal Brisbane and Women’s Hospital HREC.

Intervention

All participants were enrolled in a multidisciplinary HF disease management program which included weekly group based education sessions for 12 weeks, individual education and counselling, symptom review and medication titration supported by clinic review and telephone follow-up. Additionally, all participants received supervised center-based exercise training and a comprehensive home exercise program, prescribed and progressed by the physiotherapist and/or accredited exercise physiologist at each site. A program rolling model was employed with the aim that participants commence exercise training within six weeks of hospital discharge. The center-based exercise training program consisted of twice weekly sessions conducted in the facility’s gymnasium for 12 weeks (with 24 sessions equalling 100% attendance), followed by weekly maintenance sessions for an additional 12 weeks. Duration of training was selected on the basis that this is common practice for HF exercise training programs in Australia and was similar to previous research trials (Davidson et al, 2010; O’Connor et al, 2009). Analysis in this study was confined to the initial 12 weeks only. Programs were one hour duration and included a range of upper limb and lower limb endurance and resistance exercises in addition to warm up and cool down. Exercises were performed at an intensity of 9-14 on the rating of perceived exertion (RPE, range 6-20) scale and were monitored and progressed regularly to maintain this intensity.

Participants were also encouraged to undertake a home exercise program consisting of at least 30 minutes of moderate intensity exercise per day (RPE 9-14), for most days of the week, aiming for 150 minutes per week (ie at least 5 days/week). This included a walking program as well as individually prescribed endurance and resistance exercises performed in the home.
environment. Exercises in the home exercise program were often included in the center-based program as a means of ensuring correct exercise intensity and technique. An exercise diary was provided to each participant, and was collected and reviewed weekly by the exercise specialist, at which time an updated version with modifications and progressions was provided.

Outcomes

Change in 6MWD

The primary outcome of this secondary study was improvement in 6MWD at 12 weeks. Assessments were conducted at baseline and week 12 according to recommended procedure (Holland et al, 2014), and performed by a single research officer, blinded to allocation. The test was repeated at baseline with the best result (greatest distance), used for analysis. A single 6MWD test was performed at the 12 week assessment. For the purposes of analysis and to ensure clinical relevance of results, 6MWD data were dichotomised according to improvement (yes/ no) whereby improvement was defined as i) an increase in 6MWD at follow up by at least 30 metres (Holland et al, 2014) or ii) no decline in 6MWD if baseline distance walked was greater than 500 metres. This latter condition was included to account for the ceiling effect often observed in this test. No improvement was defined as those who did not meet the above criteria.

Exercise training program attendance

Program attendance was recorded and documented at each exercise session by clinical staff at respective facilities. Total number of sessions was collated by project staff at completion of the intervention period. Attendance frequency was defined as the total number of sessions attended during the 12 week period that the individual undertook supervised exercise training.
Data were dichotomized into “frequent” and “infrequent attendance” whereby frequent was defined as attendance at ≥12 sessions. Attendance duration was defined as the number of weeks between the first attendance and the last attendance (with no reference to any missing appointments in between) during the 12 week period. Duration thus reflected time to drop out. Data were dichotomized into two groups using a duration of six or more weeks being the cut off.

Physical activity participation

Physical activity participation was defined according to all self-reported activity performed outside of the structured exercise program, and included exercise undertaken as part of the prescribed home exercise program. Participants were provided with examples of activities that represented “moderate intensity” and the project officer clarified responses with participants to optimize accuracy. Those who participated in 150 minutes or more of moderate intensity physical activity per week in the two weeks preceding the respective assessment, were classified as being physically active whilst those who reported not achieving this target, were classified as physically inactive.

Participant characteristics

Participant characteristics such as age, ejection fraction, HF phenotype, HF presentation (new versus decompensated HF), co-morbidities and medications, were obtained from medical records and assessment items undertaken as part of the baseline physical assessment (Geriatric Depression Scale, Instrumental Activities of Daily Living scale).

Data analysis

Participant characteristics, exercise training program attendance frequency and duration, and physical activity participation at baseline and 12 weeks were summarized using standard
descriptive statistics. Association between exercise variables and improvement in 6MWD at 12 weeks was described using contingency tables and chi-square testing.

All outcomes were assessed for normality. Logistic regression was then performed to examine the independent association of these exercise variables with improvement in 6MWD at 12 weeks. Results were reported using odds ratios and 95% confidence intervals, with the level of statistical significance set at $p<0.05$. Analysis was undertaken using an intention to treat approach. To determine if missing data at week 12 was likely to significantly impact upon results, comparison was made between data from those with complete datasets and data from the whole study group (n=140), using t tests for baseline mean 6MWD and age, and a Fisher’s exact test for categorical variables.

**Results**

One hundred and forty participants were assigned to the intervention arm of EJECTION-HF and provided data for this analysis. Figure 1 demonstrates missing data at each time point. Participants with and without missing data were found to have similar characteristics (data not shown). As demonstrated in Table 1, participants were predominantly male and had a mean age of 62 years. The majority of participants had HF with reduced ejection fraction (HFrEF) and multimorbidity and disability were common.

Of the 140 participants in this study, only one person attended all 24 available sessions in the 12 week period. Fifty-seven (41%) participants attended frequently ($\geq$12 sessions) and median attendance was 9 sessions over the 12 weeks. As depicted in Figure 2, non attendance was most common in the second half of the program. At week one, the majority of participants attended at least once with 67 (48%) attending one session and 33 (24%) attending twice as per the protocol. At week 12, only half (53%) of participants attended, with 46 (33%) attending one session and 28 (20%) attending both sessions offered. The median duration of
attendance (time to drop out) was 11 weeks, with 58 (41%) participants attending for the full duration of 12 weeks, and 112 (80%) for at least 6 weeks. At baseline, 60/140 (43%) participants were physically active. At 12 weeks 92/117 were physically active, including 50 who had been physically inactive at baseline.

The association between exercise variables and improvement in 6MWD is shown in Table 2. Frequent exercise training program attendance and being physically active at 12 weeks, were both important contributors to significant improvement in 6MWD. Physical activity participation at baseline and attendance duration were not significantly associated with improvement in 6MWD and were therefore not included in the subsequent model. Results of the logistic regression model demonstrated that those who were physically active at week 12 were more likely to improve 6MWD than those not physically active at this time (OR 3.8, 95% CI 1.3-11.5, p = 0.018). Similarly, frequent attenders were more likely to improve 6MWD compared to poor attenders (OR 2.7, 95% CI 1.2-5.9, p=0.016). Those who achieved both targets were 10.3 times more likely to improve 6MWD. There was no interaction effect between these variables.

Figure 3 illustrates the proportion of participants who improved 6MWD at 12 weeks, with respect to physical activity participation and exercise training program attendance. Those individuals who attended frequently and who were physically active at 12 weeks were significantly more likely to improve 6MWD than those physically inactive at follow up (p=0.009).

**Discussion**

This secondary analysis of the EJECTION-HF trial was undertaken to describe exercise participation in people recently hospitalized with HF and to identify associations between exercise participation and improvements in 6MWD. In this study only one participant
attended all 24 exercise sessions and fewer than half of participants attended 50% of available sessions at the health facility. At 12 week follow up, close to 80% of HF participants were deemed to be physically active. Both parameters, exercise training program attendance and meeting physical activity guidelines, were strongly associated with improvements in 6MWD.

Very few studies have specifically investigated exercise participation in people recently hospitalised with HF. Attending more than one exercise session per week was not common in our participants, however compares favourably to a similar trial which aimed to enrol participants within ten days of hospital discharge (Houchen-Wolloff, Watt, Bryce, and Singh, 2016). This latter study found an exercise training program undertaken at this very early time frame to be non feasible due to poor participant uptake (Houchen-Wolloff, Watt, Bryce, and Singh, 2016).

Results from studies enrolling symptomatically stable patients suggest that poor program attendance is indeed a common problem (Collins et al, 2004; Deka, Pozehl, Williams, and Yates, 2017; Mandic et al, 2009; O'Connor et al, 2009; Park et al, 2017). In the post discharge phase, specific challenges may pose as barriers to exercise participation, potentially leading individuals to be negatively labelled as “non adherent”. This is particularly relevant for the elderly and those with multimorbidity who are often required to balance multiple competing health services at this time, or who may require readmission to hospital as a consequence of worsening symptoms. In order to account for these challenges and periods of symptom instability, HF exercise training programmes are typically longer in duration than traditional cardiac rehabilitation programmes. Results of this pragmatic trial, in which half of participants had multimorbidity or disability, suggest that whilst recruitment to the exercise program within six weeks of hospital discharge was feasible, it may be unrealistic to expect people to attend more than once per week.
That meeting physical activity guidelines was strongly associated with improvements in 6MWD is a reassuring result for people unable to attend center-based exercise training programs or for those only able to attend infrequently. These results are also supported by Sutherland et al, who similarly demonstrated a significant association between meeting physical activity guidelines and improvements in 6MWD (Sutherland, Harrison, and Doherty, 2018). In our study, those who achieved both targets of frequent program attendance and being physically active, were 10 times more likely to improve walking distance at 12 week follow up. This “dose” response has been demonstrated previously by Keteyian et al, (2012), and is a worthwhile message with which to counsel patients (Keteyian et al, 2012). For those who are able to attend exercise training programs, frequent attendance should be supported, accompanied by encouragement to undertake a home exercise program at recommended levels. This dose response may also explain the finding that programme duration was not significantly associated with improvements in exercise capacity in this study, a result previously reported by Vromen et al (Vromen et al, 2016).

An interesting finding in the current study was change in physical activity participation following the center-based program. This outcome has rarely been reported in HF exercise trials. In our study, less than half of participants were physically active at baseline, however by 12 weeks, almost 80% reported meeting this target. This exceeds results of other large center-based trials including the HF ACTION trial, in which only one third of participants were reported to achieve 120 minutes of moderate intensity exercise per week at follow up (O’Connor et al, 2009). Conducting the exercise program as a component of a comprehensive multidisciplinary disease management program, rather than a standalone intervention, may explain these findings. In the current study participants were reviewed at each exercise session attendance by HF Service clinicians, an intervention which included education, monitoring of symptoms, medication review and titration, early management of concerns and provision of
emotional support. Motivational interviewing techniques were used at each session to review and modify the center-based and home exercise programs as well as to support other behaviour changes in collaboration with the patient. Some of these strategies have previously been recommended for enhancing exercise adherence (Conraads et al, 2012; Deka, Pozehl, Williams, and Yates, 2017). It is possible that incorporating the exercise program as part of a comprehensive service, delivered in one location by a consistent team, may have enhanced individuals’ perception of benefit, thus explaining these positive findings compared to previous trials. A recent study by Liu et al, similarly recommends this model of delivery (Liu et al, 2018).

The importance of physical activity undertaken outside of the hospital environment cannot be underestimated. In addition to improving exercise capacity (Evangelista, Cacciata, Stromberg and Dracup, 2017; Sato et al, 2012; Sutherland, Harrison, and Doherty, 2018), it has also been identified as an important predictor of clinical outcomes in people with HF (Doukky et al, 2016; Keteyian et al, 2012; Sato et al, 2012; Waring, Gross, Soucier, and ZuWallack, 2017). Conversely, being physically inactive has been shown to be associated with double the risk of both all cause and cardiac mortality compared to those who are physically active (Doukky et al, 2016). Even modest leisure time activity in HF patients has been associated with improved survival (Doukky et al, 2016; Keteyian et al, 2012). This is an important message to convey to patients. Whilst higher training intensities may yield more promising results, for older patients and those with more severe symptoms or pain, exercising at even moderate intensity may be unrealistic (Haedtke et al, 2017). An approach recently proposed for those with chronic lung disease is to place emphasis on substituting sedentary time with light intensity physical activity, rather than a “one size fits all approach” with recommendations based solely on moderate to vigorous intensity exercise (Cavalheri et al, 2016; Furlanetto et al, 2017; Mesquita et al, 2017; Spruit et al, 2015). Providing clear, “real world” and achievable
recommendations with tangible outcomes may enhance exercise adherence in these patients (Back, Oberg, and Krevers, 2017; Conraads et al, 2012).

There are several limitations to our study. There is currently no consensus regarding best measurement of physical activity and data from our study were dependent upon a non validated method of self-report. Whilst we considered using accelerometers, we were concerned that this may have influenced exercise behaviour, and may have added to research burden for participants in this study. Attendance data and other outcomes may have been influenced by hospital admissions during the study period as well as other unmeasured confounders. Sample size was relatively small and the study was thus underpowered to include multiple variables in the regression analysis. It should be highlighted that important factors such as baseline characteristics, were not included in the analysis and may have influenced change in 6MWD. Findings should therefore be interpreted with caution. Results also potentially pertain to a select population due to the small sample size, however characteristics of participants were similar to those seen clinically in exercise training programs and results therefore have relevance.

This study demonstrated that meeting physical activity guidelines and attending at least one exercise training session per week were both strongly and independently associated with improvements in 6MWD. Whilst the goals of any exercise intervention should be to improve and maintain exercise capacity, equally important is to promote positive and sustainable exercise behaviours that optimize clinical outcomes in the long term (Conraads et al, 2012; Cooper et al, 2015; Doukky et al, 2016). Services should be tailored for best effect, with interventions directed towards assisting individuals to be physically active, acknowledging that the time required to achieve this change may vary among individuals. Flexible models which account for periods of instability should be encouraged, particularly in the post
hospitalization phase. Limited data is currently available on how age, gender, HF characteristics and other variables may impact upon exercise adherence in patients with HF. Future studies should thus explore this in more detail and characterize potential subgroups for whom a more tailored approach may be appropriate. In so doing, studies should continue to identify strategies which may assist individuals to attend center-based exercise training programs where possible, to improve physical activity participation and to potentially lessen sedentary behaviour. The impact of illness and rehospitalisation on exercise participation following discharge should also be explored. Finally, studies should explore safety and efficacy of alternative options for exercise training as a means of providing further opportunities for individuals to engage in sustainable and meaningful activity.
References


Table 1. Participant characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Participants n=140</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean years (SD)</td>
<td>62 (15)</td>
</tr>
<tr>
<td>Male gender, n (%)</td>
<td>108 (77)</td>
</tr>
<tr>
<td>EF &lt;40%, n (%)</td>
<td>108 (77)</td>
</tr>
<tr>
<td>New diagnosis HF, n (%)</td>
<td>82 (58.6)</td>
</tr>
<tr>
<td>NYHA, n (%)</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>25 (18)</td>
</tr>
<tr>
<td>II</td>
<td>73 (52)</td>
</tr>
<tr>
<td>III</td>
<td>26 (19)</td>
</tr>
<tr>
<td>IV</td>
<td>16 (11)</td>
</tr>
<tr>
<td>HF aetiology, n (%)</td>
<td></td>
</tr>
<tr>
<td>Ischaemic</td>
<td>52 (37)</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>25 (18)</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>38 (27)</td>
</tr>
<tr>
<td>Other</td>
<td>25 (18)</td>
</tr>
<tr>
<td>AF present, n (%)</td>
<td>53 (38)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>88 (62.9)</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>48 (34.3)</td>
</tr>
<tr>
<td>Condition</td>
<td>Count (Percentage)</td>
</tr>
<tr>
<td>----------------------------------------------------------------------------</td>
<td>--------------------</td>
</tr>
<tr>
<td>COPD present, n (%)</td>
<td>34 (24.3)</td>
</tr>
<tr>
<td>Chronic renal impairment, n (%)</td>
<td>31 (22.1)</td>
</tr>
<tr>
<td>Anaemia present, (Hb &lt;120 g/L males and &lt;110 g/L females), n (%)</td>
<td>34 (27)</td>
</tr>
<tr>
<td>Depression present (GDS &gt;5), n (%)</td>
<td>46 (35)</td>
</tr>
<tr>
<td>Multimorbidity CCI ≥ 3, n (%)</td>
<td>66 (47)</td>
</tr>
<tr>
<td>Disability present (IADL &gt;1), n (%)</td>
<td>73 (52)</td>
</tr>
<tr>
<td>Baseline 6MWD, mean metres (SD)</td>
<td>361 (127)</td>
</tr>
<tr>
<td>Medications</td>
<td></td>
</tr>
<tr>
<td>ACEi/ ARB</td>
<td>125 (89.3)</td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>127 (90.7)</td>
</tr>
<tr>
<td>MRA</td>
<td>52 (37.1)</td>
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<tr>
<td>Loop diuretic</td>
<td>119 (85.0)</td>
</tr>
<tr>
<td>Digoxin</td>
<td>34 (24.3)</td>
</tr>
</tbody>
</table>

ACEi, Angiotensin converting enzyme inhibitor; AF, Atrial fibrillation; ARB, Angiotensin receptor blocker; CCI, Charlson comorbidity index; COPD, Chronic obstructive lung disease; EF, Ejection fraction; GDS, Geriatric depression scale; Hb, Hemoglobin; IADL, Instrumental activities of daily living; MRA, Mineralocorticoid receptor antagonist; NYHA, New York Heart Association
### Table 2. Association between exercise variables and improvement in 6MWD

<table>
<thead>
<tr>
<th>Exercise Variable</th>
<th>Improved 6MWD, n (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attendance frequency ≥12 sessions</td>
<td>34/52 (65.9)</td>
<td>0.003</td>
</tr>
<tr>
<td>Attendance frequency &lt;12 sessions</td>
<td>23/62 (37.1)</td>
<td></td>
</tr>
<tr>
<td>Attendance duration ≥6 weeks</td>
<td>53/101 (52.5)</td>
<td>0.141</td>
</tr>
<tr>
<td>Attendance duration &lt;6 weeks</td>
<td>4/13 (30.8)</td>
<td></td>
</tr>
<tr>
<td>PA baseline ≥150 minutes</td>
<td>44/88 (50)</td>
<td>0.347</td>
</tr>
<tr>
<td>PA baseline &lt;150 minutes</td>
<td>53/122 (43.4)</td>
<td></td>
</tr>
<tr>
<td>PA at 12 week follow-up ≥150 minutes</td>
<td>80/161 (49.7)</td>
<td>0.046</td>
</tr>
<tr>
<td>PA at 12 week follow-up &lt;150 minutes</td>
<td>16/48 (33.3)</td>
<td></td>
</tr>
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</table>

6MWD, 6 minute walk distance, PA: Physical activity
Total participants
n = 140

Baseline assessment
Attendance data = 140
Physical activity participation data = 140
6MWD data = 140

Intervention

12 week follow up
Attendance data = 140
Physical activity participation data = 117
6MWD data = 114

Died = 1
Too unwell = 8
Unable or unwilling to attend assessment = 11
Unable to contact = 4
Missing data = 2

Figure 1. Flow diagram of participants and available data at baseline and 12 week follow up

6MWD, 6 minute walk distance
Figure 2. Percentage of participants who attended the exercise programme according to session frequency and week of attendance.
Figure 3. Percentage of participants who improved 6MWD at week 12 according to exercise programme attendance frequency and being physically active at 12 weeks.