Personalised home-based physical activity intervention in older adults with Heart Failure.

Research Protocol
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Background

Heart Failure (HF) is one of the most common forms of chronic heart condition and affects nearly 1 million people in the UK [1, 2]. The incidence and prevalence of HF have increased steeply as a result of (1) improved prognosis of coronary artery disease, (2) ageing of the population and (3) better medical treatments [3-5]. Aside from the obvious individual burden, HF also accounts for 1 million inpatient bed days - 2% of all NHS inpatient bed-days and 5% of all emergency medical admissions to hospital [2, 3]. It costs the NHS nearly 2% of its annual budget (around £625 million) [2, 3]. Hospital admissions because of HF are projected to rise by 50% over the next 25 years [2, 3].

Evidence-based guidelines have been developed to improve diagnosis and treatment of HF [2, 6, 7]. These position physical activity and exercise therapy is a cornerstone of clinical management of Heart Failure. Evidence from meta-analyses shows that exercise improves functional capacity, quality of life, reduce symptom burden, reduce readmissions to hospital and improve survival in HF [8-11]. Exercise reverses the left ventricular remodelling and improves cardiac function at rest and during exercise [12-14]. Current guidelines from the UK, EU, and USA recommend exercise as an effective and safe intervention for HF (recommendation class I) [6, 7, 15].

Despite the clear recommendations, only a small number of people affected by HF participate in cardiac rehabilitation [1]. Only 2% of people who participated in cardiac rehabilitation in the UK were referred because of heart failure [15]. Recent cross-national survey from England, Wales, and Northern Ireland reported that people with HF as a primary diagnosis are excluded from most cardiac rehabilitation programmes due to lack of resources and direct exclusion from local commissioning agreements [16]. In addition, a significant number of people do not accept the invitation to attend cardiac rehabilitation with the main reasons being difficulties in regularly attending centre-based cardiac rehabilitation sessions, work or domestic commitments and reluctance to take part in group-based classes [17] [18].

Home-based exercise cardiac rehabilitation programmes have been introduced in an attempt to widen access and participation as an alternative to supervised centre-based rehabilitation [19]. Home-based exercise programmes seem to be equally effective as centre based programmes *in people with coronary artery disease* i.e. following myocardial infarction and revascularisation [18-20]. It remains to be determined whether home-based exercise programmes deliver benefit to people with chronic HF.

Aim and Objectives:

To design and evaluate a home-based physical activity intervention for adults with HF in order to improve participation in cardiac rehabilitation. This aim will be achieved through the following 3 objectives: (1) define current levels of physical activity and sedentary behaviour and their clinical correlates in HF, (2) co-design a personalised home-based physical activity intervention with patients, *and* (3) determine the effect of the home-based physical activity intervention.

Methods/Design

Design

In order to design and evaluate a home-based physical activity intervention for older adults with heart failure, the research programme will have 2 research phases.

Phase 1 – Qualitative Research using the Focus Group approach. Ten to fifteen older adults with chronic heart failure will take part in 3 focus groups to help identify i) views on performing home-based physical activity interventions, ii) potential barriers and facilitators to increasing physical activity levels; and iii) motivational incentives to increase and maintain appropriate physical activity level and introducing behavioural change. The focus groups will be conducted before, during and after the intervention by a HCPC registered Health Psychologist at the NIHR Clinical Research Facility, Royal Victoria Infirmary, Newcastle upon Tyne.

Phase 2 – A single arm, feasibility and pilot study design will be used to assess the effect of a home-based physical activity intervention in older people with chronic heart failure due to systolic dysfunction. Participants will be recruited through the Royal Victoria Infirmary and Freeman Hospitals in Newcastle and will be screened prior to commencement of the study to assess eligibility. Eligible participants will then be given clinical and physiological baseline assessments. Following baseline assessments, participants will undergo a 12-week personalised home-based physical activity intervention. The goal is that each study participant increases activity levels (e.g. daily number of steps) from the baseline. The target is that participants reach the activity level that is at least 2000 steps per day more from baseline, as this increment is associated with a significant 10% reduction in cardiovascular events in individuals at high cardiovascular risk [21]. A commercial physical activity monitoring device (pedometer i.e. step counter; Omron, USA) will be provided for use throughout the study to allow participants to self-monitor activity levels to enhance motivation.

Sample size

A total of 40 participants with heart failure due to left ventricular dysfunction will be recruited from Newcastle Royal Victoria Infirmary and Freeman Hospital.

Eligibility criteria

Inclusion criteria:

1. Older adults (>60 years of age) with chronic heart failure due to left ventricular systolic dysfunction
2. Clinically stable for at least 6 weeks prior to screening
3. Receipt of optimal medical treatment
4. Able to walk and perform activities of daily living independently
5. New York Heart Association functional class II-IV
6. Left ventricular ejection fraction <40%
7. Willingness to undertake a physical activity intervention
8. Willingness to visit the clinical research facility on 2 separate occasions.
9. Ability to read, write and converse in English without the support of an interpreter.

Exclusion criteria:

1. Severe aortic stenosis
2. Severe cardiac arrhythmias
3. Myocardial infarction, percutaneous coronary intervention and/or bypass graft surgery over the past 3 months
4. Clinically unstable with recent changes in medication
5. Severely obese i.e. body mass index >35
6. Implanted with left ventricular assist device
7. Current participation in cardiac rehabilitation programme or in the past 3 months
8. Inability to provide informed consent.

Recruitment procedures

Patients will be recruited from Heart Failure Clinics of Newcastle Royal Victoria Infirmary and Feeman Hospital run by Drs Skinner, Bailey, and MacGowan. Eligible patients will be contacted by the member of the study team. An information sheet will be mailed out upon request, and should individuals wish to take part in the study, a screening visit will be arranged where informed consent will be obtained. Consent forms will be signed by the participant and countersigned by a member of the study team.

Research Visits – In addition to attending the focus group, eligible participants will attend the Clinical Research Facility of the Royal Victoria Infirmary for two separate visits i.e. before and after the 12-week intervention. Participants will be contacted via email, telephone or spoken to in person to discuss the project and will be taken through the information sheet to ensure they understand the nature of the study. Each visit will last 3.5-4 hours and includes one hour break for breakfast. The following clinical investigations will be performed during the visits 1 and 2:

i) Consent and Screening Questionnaires (30 minutes).

- Patients will be provided with the opportunity to ask further questions and requested to provide written informed consent. They will then be asked to complete Physical Activity and Quality of Life measures i.e. Minnesota Living with Heart Failure Questionnaires.

ii) Blood Sample(15 min).

- After an overnight fast, the blood sample will be taken from the antecubital vein. The blood sample will be assessed for brain natriuretic peptides (NTproBNP), lipid profile (total cholesterol, HDL-cholesterol, LDL-cholesterol), triglycerides, glucose, HbA1c, markers of renal function (urea, creatinine, eGFR), markers of inflammation (TNFα, CRP), endothelial progenitor cells, and circulating endothelial cells.

iii) Body composition using non-invasive air displacement plethysmography (15 min).

- The amount of fat and muscle in the body will be assessed using air displacement plethesmography(BodPod). The participant will sit quietly in the bodpod wearing swimwear for 2 minutes.

iv) Breakfast (60 min)

- As participants are coming following an overnight fast, they will be provided with a light breakfast consisting of a toast and orange juice.

v) Electrocardiography (ECG)(10 min).

- The ECG will be performed using a standard 12-lead electrocardiogram in supine position.

vi) Echocardiography for assessment of cardiac structure and function using non-invasive Doppler ultrasound (30 min).

- An echocardiogram is an ultrasound scan of the heart. Participant will be undressed to the waist and asked to lie on the couch. A probe (e.g. thick blunt pen) is placed on the

chest. Lubricating jelly is put on the chest to form good contact between the probe and skin. The probe is connected by a wire to the ultrasound machine and monitor. Pulses of ultrasound are sent from the probe through the skin towards the heart. The ultrasound waves then echo ('bounce back') from the heart and various structures in the heart.

vii) Arterial stiffness using non-invasive pulse wave analysis methods (10 min).

- Arterial stiffness, as a measure of arterial function, will be assessed using the SphygmoCor device which allows for both pulse wave analysis and pulse wave velocity to be performed non-invasively using the gold standard techniques. The measurement is simple and painless, taking only a few minutes to perform. While the participant is in a comfortable supine position, the researcher will place a tonometer (pencil-like sensor) gently against the wrist and will record blood pressure signal from the pulse.

viii) Cardiac autonomic function (10 min).

- Cardiac autonomic function i.e. heart rate and blood pressure variability will be assessed using non-invasive methods integrated into the TaskForce device. Using electrocardiogram and continuous blood pressure monitoring with a finger cuff under resting supine condition computer will assess heart rate variability and blood pressure variability.

ix) Progressive cardiopulmonary exercise test (30 min).

- A progressive exercise test will be undertaken to assess non-invasively oxygen extraction efficiency, peak oxygen uptake, and ventilatory threshold. Patients will be asked to wear facemask to collect and analyse expired gasses. An ECG, blood pressure, and cardiac output (using non-invasive bioreactance method that utilise 4 dual electrodes placed on the back side of the thorax) will also be performed (resting and during the exercise). In brief, using a cycle ergometer the progressive exercise test involves maintaining a pedal frequency of 60-70 revolutions per minutes with work increasing at 1 minute intervals. The test will be terminated when the patient is unable to maintain pedal frequency above 60 rpm or the patient voluntary terminates the test. Exercise testing will be performed by DH and DGJ.

DH and DGJ have experience in conducting exercise tests in patients with various clinical conditions including those with heart failure. DH and DGJ are first aid, CPR and defibrillator trained. DH or DGJ will be accompanied by one other first aid trained supervisor for all testing sessions.

x) Physical activity monitoring.

- At the end of all investigations the patient will be provided with the small, unobtrusive accelerometery monitor (i.e. wrist-watch or arm-band like device and pedometer for counting daily number of steps) to assess physical activity level over a 7-day period. The monitor will be returned to the research team through the post in provided pre-paid envelope.

Intervention

The aim of the intervention is that study participants increase their overall daily physical activity level by at least 2000 steps from baseline (e.g. walking at low intensity for approximately 30 minutes). This can be divided into several bouts of shorter duration throughout the day e.g. 3 x 10 min or similar with overall aim that at the end of the each day pedometer indicates at least 2000 steps more from the average daily number of steps obtained at baseline.

Patients will be asked to complete a daily exercise diary which will be analysed and discussed on a weekly basis (as appropriate) with the member of the research team. Each exercise session will include a warm-up period, the main part of the training and a cool-down period that will be explained during the visit 1. To control for exercise intensity patients will be instructed to use standardised Borg Scale (0-20) to rate perceived exertion aiming for achieving the levels between 11 – 13 (easy-light-to somewhat hard). The exercise prescription will be progressed individually as conditioning took place, with the emphasis placed on volume of activity i.e. duration before intensity.

End of the Study

At the end of the study all participants will be provided with information about any changes observed in their cardiovascular and physiological function. This will be communicated by letter mailed to the participants home address and will also include an invitation to attend a volunteer feedback evening at the Clinical Research Facility where the overall results of the study will be presented. The study will be completed when study participants have completed the study and have attended the final visit at week 12.

Statistical Analysis

Data from this pilot study will be analysed and used to inform sample size requirements of a larger scale study. The sample size of 40 will provide high power to the study (β=0.82) to detect significant change (α=0.05) in a clinical hallmark of HF i.e. exercise intolerance (peak O_2 consumption of 3 ml/min/kg) following the intervention. Prior to statistical analysis, data will be checked for univariate and mulitivariate outliers using Z-distribution cut-offs and

Mahanolobis distance test. Normality of distribution will be assessed using a Kolmogorov-Smirnov test. T-tests for paired samples will be used to assess the effect of intervention on outcomes measures. The relationship between physical activity, clinical and physiological variables will be assessed using Pearson's product moment coefficient of correlation or Spearman's rank correlation coefficient, as appropriate. Statistical significance was indicated if $P<0.05$.

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