Feasibility of Home-based Exercise Program for Adults With Cystic Fibrosis

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This was a randomized controlled pilot and feasibility study or a home-based exercise program among PwCF. Participants were recruited from The University of Kansas Health System (TUKHS) CF outpatient clinic. All study procedures were approved by the University of Kansas Medical Center Institutional Review Board and written informed consent was obtained from all participants (IRB number CR00020120).

Participants

Adults with CF (two confirmatory CF mutations or sweat chloride > 60 mmol/L) who were 18 years of age or older and stable on HEMT elexacaftor/tezacaftor/ivacaftor (ETI) for ≥ 3 months with clearance from their CF physician were eligible to participate. Exclusion criteria included completion of ≥ 150 minutes of structured exercise per week for the last X time, pregnancy, post solid organ transplant, active treatment for mycobacterial infections, oxygen dependent at rest or with exercise, FEV_1 < 40% of predicted, clinical evidence of cor pulmonale, untreated arterial hypertension (resting systolic blood pressure >140 mm Hg, diastolic blood pressure > 90 mmHg), systolic blood pressure less than 90 mm Hg while standing, congestive heart issues, active treatment for Allergic Bronchopulmonary Aspergillosis (ABPA), pulmonary exacerbation within 4 weeks prior to Day 1, or changes in therapy (including antibiotics) for pulmonary disease within 4 weeks prior to Day 1, significant hemoptysis within 4 weeks prior to Day 1 (≥5 mL of blood in one coughing episodes or >30 mL of blood in a 24 hours period), and ongoing participation in an investigational drug study within 60 days prior to Day 1.

Eligible participants who consented were randomized 1:1 via a computer-generated randomization technique to either the intervention or control group. Participant demographics, incremental meter shuttle walk test (IMSWT), spirometry, xenon magnetic resonance imaging (Xe-MRI), the Cystic Fibrosis Questionnaire Revised (CFQ-R), and surveys regarding physical activity were completed at baseline and upon study completion. Semi-structured interviews evaluating exercise were completed in the intervention group at the conclusion of the follow-up visit.

Intervention/Exercise Protocol

Those randomized to the intervention group were assigned to an exercise coach and asked to wear a wrist-worn Garmin vivosmart 4 actigraph during physical activity. Participants were asked to complete 12 weeks of progressive home-based exercise program in a target heart rate zone, with an exercise target of 60 minutes in weeks 1 and 2, 90 minutes in weeks 3 and 4, 120 minutes in weeks 5 through 8, and 180 minutes in weeks 9 through 12. Target heart rate zone was calculated using the heart rate reserve (HRR) method for moderate activity levels as described by the American College of Sports Medicine (ACSM), which uses an intensity factor of 40-85% of the maximal heart rate achieved during the IMSWT. Exercise coaches contacted participants weekly by phone, text, or email to discuss

strategies for reaching exercise minute goals and provide personalized feedback regarding exercise motivations and barriers. Physical activity was participant-determined and based on individual preferences, lifestyle, and resource availability.

The control group received standard-of-care instructions regarding exercise and instruction on how to access beamfeelgood, an online repository of exercise videos available free of charge for PwCF.

Outcome Measures

The IMSWT was used as a surrogate for CR-fitness as it has shown construct validity and predictive value for VO_{2max} in adult CF patients. Testing was conducted according to the protocol outlined by Singh et al. Distance and maximal heart rate were collected at the end of the IMSWT.

Adherence to exercise was calculated as the number of exercise minutes completed in the target heart rate zone each week/weekly target exercise minutes. Participants were considered to be adherent if they completed ≥70% of weekly exercise minutes for ≥70% of the 12-week intervention.

Spirometry was obtained from TUKHS CF outpatient clinic. Forced expiratory flow in one second (FEV1) was collected from TUKHS electronic medical record. FEV1 is expressed as %predicted (ppFEV1) using NHANES III spirometric reference ranges.

The CFQ-R is a valid and reliable self-administered questionnaire composed of 44 items on 12 generic and disease-specific domains and is used to assess health-related quality of life (HrQoL) in adults with CF. (citation) Overall CFQ-R score and each domain score were collected.

The Barriers to Physical Activity questionnaire assesses barriers to participating in physical activity and asks participants to rank 15 items on a 5-point Likert scale from “never” to “very often” limiting physical activity. Overall barrier score and each item score were collected.

Xe-MRI was used to measure ventilation and gas exchange. Xe-MRI was completed prior to the IMSWT for all study participants by a minimum of 30 minutes. Isotopically enriched (90% ^{129}Xe) xenon gas (Linde Specialty Gases) was polarized to >25% using a Polarean 9820 xenon hyperpolarizer (Polarean Imaging Plc., Durham, NC). The total dose volume delivered to participants was equal to 20% of FVC measured at the baseline study visit. Participants were imaged using a 3T Skyra MRI scanner (Siemens, Erlangen, Germany) using a flexible transmit/receive ^{129}Xe vest coil (Clinical MR Solutions, LLC, Brookfield, WI). Calibration data was analyzed in real-time using a home-built MATLAB (version 2020A, MathWorks, Natick MA) program and the outputs used for subsequent imaging. Following calibration, every participant was imaged using 3D ventilation imaging. Within the same breath, a

geometry-matched ^{1}H anatomic image set was acquired to be used for image quantification.

Xe-MRI images were quantified using an automated pipeline to quantify ventilation defect percent (VDP). VDP was calculated using the mean anchored linear binning approach with a threshold of 60%. VDP was an exploratory endpoint for this study.

Data Analysis

To achieve 80% power at an α level of 0.05 (two-sided), 12 participants were needed in each group to detect an effect size of 1.2. A target enrollment of 15 per group (n=30 total) was set to account for attrition.

Data is presented as mean ± SD, categorical data is presented as a percentage. Baseline between group differences were analyzed with a Wilcoxon Mann-Whitney test for continuous variables and a Fisher's exact test for categorical variables, as appropriate. No between group differences were found for demographic or baseline measures. Group differences for all outcome measures were assessed using a Wilcoxon Mann-Whitney test. An intention-to-treat approach was used for participant baseline characteristics. Participants with missing post-intervention data were excluded from group difference analyses.

All statistical analyses were performed using SAS v9.4. All comparisons were two-sided with the level of significance set at $p < 0.05$.