Received: 3 January 2017 | Revised: 21 August 2017 | Accepted: 19 October 2017

DOI: 10.1111/chd.12562

ORIGINAL ARTICLE

WILEY Congenital Heart Disease

Home-based interval training increases endurance capacity in adults with complex congenital heart disease

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Funding information
Swedish Heart-Lung Foundation, Grant/Award Numbers: 20100355, 20130472; Heart Foundation of Northern Sweden; Research Foundation of The Swedish Heart and Lung Association, Grant/Award Number: E116/12, E115/13, E129/14; Research Foundation of Healthcare Professions within Cardiology, Umeå University; Västerbottens läns landsting, Umeå, Sweden, Grant/Award Number: 316351; and ALF-LUA grants at Sahlgrenska University Hospital, Göteborg, Sweden

Abstract

Objective: The beneficial effects of exercise training in acquired heart failure and coronary artery disease are well known and have been implemented in current treatment guidelines. Knowledge on appropriate exercise training regimes for adults with congenital heart disease is limited, thus further studies are needed. The aim of this study was to examine the effect of home-based interval exercise training on maximal endurance capacity and peak exercise capacity.

Design: Randomized controlled trial.

Methods: Twenty-six adults with complex congenital heart disease were recruited from specialized units for adult congenital heart disease. Patients were randomized to either an intervention group—12 weeks of home-based interval exercise training on a cycle ergometer (n = 16), or a control group (n = 10). The latter was instructed to maintain their habitual physical activities. An incremental cardiopulmonary exercise test and a constant work rate cardiopulmonary exercise test at 75% of peak workload were performed preintervention and postintervention.

Results: Twenty-three patients completed the protocol and were followed (intervention n = 13, control n = 10). Postintervention exercise time at constant work rate cardiopulmonary exercise test increased in the intervention group compared to controls (median[range] 12[−4 to 52]min vs 0 [−4 to 5]min, $P = .001$). At incremental cardiopulmonary exercise test, peak VO_2 increased 15% within the intervention group ($P = .019$) compared to 2% within the control group ($P = .8$). However, in comparison between the groups no difference was found (285[−200 to 535] ml/min vs 17 [−380 to 306] ml/min, $P = .10$). In addition, peak workload at incremental cardiopulmonary exercise test increased in the intervention group compared to controls (20[−10 to 70]W vs 0[−20 to 15]W, $P = .003$).

Conclusion: Home-based interval exercise training increased endurance capacity and peak exercise capacity in adults with complex congenital heart disease. Aerobic endurance might be more relevant than peak oxygen uptake with regard to daily activities, and therefore a more clinically relevant measure to evaluate.

KEYWORDS
adult, cardiopulmonary exercise testing, congenital heart disease, constant work rate, exercise training, interval training

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1 | INTRODUCTION

During the past decades there have been substantial improvements in survival and reduction in the need of reoperations for adults with congenital heart disease (CHD), especially among those with more complex lesions.[1–3] There is a well-known impairment in exercise capacity in these patients compared to healthy controls.[4,5] To what extent this impairment is due to abnormal cardiovascular physiology, per se, or to other factors such as physical inactivity or lack of exercise training, that is, deconditioning, is unknown. Furthermore, reduced exercise capacity is an important prognostic predictor of cardiovascular morbidity and mortality.[6] In addition, impaired muscle function has been observed, especially in adults with CHD that have complex lesions.[7–10] According to current recommendations of the European Society of Cardiology, adults with CHD are encouraged to be physically active and exercise training should be prescribed individually.[11] However, due largely to the low numbers of studies on effects of exercise training in adults with CHD, there are no specific recommendations regarding training mode, intensity, duration, and frequency.[12,13] Previous studies show that exercise training seems to be safe and to have positive effects on aerobic exercise capacity without adverse effect on ventricular function.[14–21] Home-based continuous moderate exercise training on an cycle ergometer increased the exercise capacity in adults with a systemic right ventricle.[17] In patients with acquired heart failure, interval training was shown to improve exercise capacity more than continuous moderate exercise training.[22] Interval training at moderate to high intensity (75%–95% of maximum HR) was also reported to be safe and increase exercise capacity in these patients.[15,18] To improve adherence to study protocol, home-based exercise training has been used in a number of previous studies.[17,23,24]

Incremental cardiopulmonary exercise testing (incremental CPET) on a cycle ergometer or treadmill is frequently used and often considered the “gold standard” when evaluating aerobic exercise capacity and change in aerobic capacity after intervention.[25,26] Changes in peak aerobic capacity, total exercise time and peak work load are variables commonly used to report study results.[12] Constant work rate CPET is a method commonly used to evaluate endurance exercise capacity in patients with chronic obstructive pulmonary disease (COPD)[27] and it has emerged as the most responsive test method to evaluate change in exercise capacity in these patients after rehabilitation intervention.[28] At present, this test has not been used to evaluate outcome of exercise training in the setting of adult CHD.

The present study was a randomized controlled trial that used CPET aimed to evaluate the effect of home-based interval exercise training on submaximal exercise capacity (endurance) and peak exercise capacity (peak work load, peak oxygen uptake) in adults with complex CHD. The hypothesis was that interval training increases endurance capacity as well as peak exercise capacity in an intervention group compared to a control group.

2 | METHODS

2.1 | Study population

Twenty-six patients (13 women) with complex CHD and reduced exercise capacity were recruited from specialized units for adults with CHD in the northern health care region (Umeå) and the region of Västra Götaland (Göteborg) in Sweden. The inclusion criteria were complex CHD, as defined by Erikssen et al.,[1] (eg, palliated with variants of Fontan procedure [Fontan/TCPC], pulmonary atresia [PA], tetralogy of Fallot [ToF], congenitally corrected transposition of the great arteries [ccTGA], dextro-transposition of the great arteries repaired with Mustard or Senning procedure [d-TGA]), clinically stable condition over the past 3 months, adult age (≥18 years of age), and informed consent. The patients with PA, as well as those with ToF, had undergone surgical repair and were not cyanotic. The exclusion criteria were present strategy for executing exercise training ≥ 2 times/week aimed at increasing or sustaining exercise capacity, arrhythmia or other adverse events (eg, important symptoms, drop in blood pressure) at CPET, clinically relevant arrhythmia, intellectual disability or mental illness affecting independent decision making, extracardiac disease affecting physical activity, peak VO_2 >30ml/kg/min at run-in CPET, or no internet access. At the time of screening (October 25, 2012) the outpatient register of CHD in the northern health care region, 391 patients were registered. Seventy-seven patients met the inclusion criteria of complex CHD. Of these, 39 patients met at least one exclusion criteria. Thus, 38 patients were eligible and were asked to participate; 17 declined participation, 1 was excluded due to arrhythmia (short periods of atrial fibrillation) and 1 was excluded due to peak $VO_2 \geq 30$ ml/kg/min at run-in CPET and 19 (53%) were finally included. There were no differences regarding age and sex between those who declined participation and those who participated. In the region of Västra Götaland, a convenience sample was collected, that is, when patients fulfilling the inclusion criteria were scheduled for a regular follow-up visit they were asked to participate. Thus, these patients were not strictly consecutively recruited. Eight patients were tested with run-in CPET, of these 1 was excluded due to arrhythmia. This gave an additional 7 patients. Finally, a total of 26 patients were included and were randomized to an exercise-training group, that is, intervention group (n = 16), or a control group (n = 10). Two patients that had been randomized to the intervention group discontinued study participation due to personal reasons. For another patient, the exercise training was discontinued after 14 training sessions due to the patient experiencing discomfort and possible arrhythmia. Therefore, 23 patients consisting of 13 in the intervention group and 10 in the control group were followed after intervention. All patients gave their written informed consent for participation. The study was approved by the regional Ethics Review Board in Umeå (Dnr 2011-51-31 M, 2011-03-29, and 2012-143-32 M, 2012-04-04).

2.2 | Exercise capacity

At the incremental CPET peak VO_2, peak work load, respiratory exchange ratio (RER) and peak heart rate were registered.[25] To ensure standardization, the participants were instructed that when rating ≥17 (very hard) on the Borg Rated Perceived Exertion scale,[29] this corresponded to perceived exertion of "not coping with an additional increase of work load." The subsequent endurance test, constant work rate CPET, was performed at 75% of peak work load that had been achieved at the initial incremental CPET. The exercise test duration was the main outcome.[27,30] In one patient in the intervention group, the postintervention constant work rate CPET was not performed due to technical issues. Therefore, for this patient we only used the incremental CPET data. For pre- and postexercise tests the Jaeger Oxycon Pro CareFusion (GmbH, Hoechberg, Germany) or Schiller CS-200 Ergo-spirometry (Schiller AG, Baar, Switzerland) was used for analysis of breathing-gases.

2.3 | Randomization process

The present study was a two-armed randomized controlled trial. Patients were randomly assigned to intervention or control group in the ratio of 2:1 that was applied by computer generated block randomization. The group allocation sequence was kept in an opaque, sealed, and stapled envelope to prevent prior knowledge, and was revealed to patients and researchers after completion of run-in tests. At the first center, the technicians performing the tests and the physician (MH) analyzing the tests were blinded for group allocation. Furthermore, the patients were instructed not to reveal their group allocation. At the second center, the investigators were not blinded. However, the tests strictly followed the prespecified protocol.

2.4 | Exercise training protocol

The exercise training was home-based and was performed three times a week for 12 weeks on a cycle ergometer with a manually adjusted brake system (Tunturi T 20/Tunturi, Tunturi- Hellberg Oy Ltd, Åbo, Finland or Bremshey BF3, Escalade Int. Ltd, Nottingham, UK). The time between completion of the run-in tests, and start of intervention was approximately 1 week due to delivery of the cycle ergometers. To individually adjust the intensity of the exercise training protocol, the training heart rate (THR) was calculated according to the Karvonen method based on the individual peak heart rate.[31] In addition to the heart rate intervals, patients were instructed to achieve perceived exertion corresponding to BORG 15–16.[29] All patients randomized to exercise training received one occasion with familiarization training. The exercise training had an initial 8 min warm-up without load or with very low load. During the first 2 weeks the protocol consisted of three intervals at $THR_{75\%\text{-}80\%,}$ and thereafter four intervals. The duration of the intervals was also individually adjusted according to total exercise time during the initial constant work rate CPET. When the total time at constant work rate CPET was less than 5 minutes, the interval time was calculated as total exercise time minus 1 minute. The maximum interval time was 5 minutes. The intervals were separated by an active recovery periods of 3 minutes without load or with very low load (Supporting Information Figure S1). During the exercise training sessions, participants wore a heart rate monitor (Polar RS 300X, Polar Electro Oy, Kempele, Finland). The registered heart rate was regularly transferred to a personal webpage that was accessed by the physiotherapist and participant. A weekly contact by phone was used to promote compliance, to provide feedback, and, when appropriate, to increase training time if a shorter interval time than 5 minutes. The participants were instructed to pay attention to symptoms such as dizziness, palpitations, chest pain, and other experiences of discomfort, and if these occurred, abort exercise and contact investigators. The maximum number of training sessions was 36 and the goal was that every participant should complete a minimum of 28 (78%) sessions. The patients randomized to control group were instructed to continue with their habitual physical activities.

2.5 | Questionnaires

In addition to exercise test data, self-reported quality of life was evaluated using the EuroQol Vertical Visual Analogue Scale (EQ-VAS).[32] The Hospital Anxiety and Depression scale (HADS)[33,34] was used for assessing prevalence of anxiety and depression. Finally, self-efficacy for exercise was evaluated using the Exercise Self-Efficacy Scale (ESE).[35] All three scales are validated and were used preintervention and postintervention.

2.6 | Statistics

The data were tested for normality. Data are presented as mean ± 1 standard deviation (SD) or median with range (min-max). Differences in means, ranks, and ratios were tested by Student's *t* test, Mann-Whitney *U* test, or chi-square test as appropriate. Paired samples *t* test and Wilcoxon's signed ranks test were applied for within group comparisons. The null-hypothesis was rejected for P values $< .05$. All calculations were performed using SPSS 22 (IBM, Armonk, NY, USA).

3 | RESULTS

Twenty-three patients were analyzed after follow-up that included 13 in the intervention group and 10 in the control group. There were no differences in baseline data between the intervention group and control group (Tables 1–3). In the population, the mean predicted peak heart rate was $88\% \pm 7.5\%$ and the mean predicted peak VO_2 was $72\% \pm 13.7\%$. Moreover, there were no differences between intervention group and control group regarding these data.

3.1 | Exercise capacity

The median test duration at constant work rate CPET increased 89% post intervention in the intervention group compared to no change in the control group (median[range] 12[−4 to 52] min vs 0[−4 to 5] min, $P = .001$). Furthermore, the peak workload (20[−10 to 70] W vs 0[−20 to 15] W, $P = .003$) at incremental CPET increased post intervention in the intervention group compared to the controls. The peak VO_2 (ml/min) at incremental CPET increased 15% within the intervention group ($P = .019$) compared to no change (2%) within the control group ($P = .8$). The results were similar regarding VO_2 indexed for body

TABLE 1 Descriptive data on included patients

		All patients (n = 23)	Intervention group (n = 13)	Controls (n = 10)	*P* value
Sex					
M	n (%)	12(52)	8(62)	4(40)	.31
F	n (%)	11(48)	5(39)	6(60)	
Age, years	Median(IQR)	30.1(22.9–36.6)	31.3(26.9–36.6)	26.3(22.9–35.6)	.38
Height, m	Mean ± SD	1.72(0.10)	1.72(0.09)	1.72(0.10)	.85
Weight, kg	Mean ± SD	77(15)	77(10)	76(21)	.90
BMI, kg/m^2	Mean ± SD	25.8(3.9)	26.0(3.6)	25.5(4)	.77
Diagnosis	n (%)				
ToF		5(22)	4(31)	1(10)	.19
ccTGA		3(13)	3(23)	0(0)	
d-TGA		5(22)	2(15)	3(30)	
TCPC		5(22)	3(23)	2(20)	
PA		2(9)	0(0)	2(20)	
Complete AV-septal defect		1(4)	0(0)	1(10)	
Ebstein		1(4)	0(0)	1(10)	
Miscellaneous		1(4)	1(8)	0(0)	
Surgical intervention, yes	n (%)	21(91)	11(85)	10(100)	.19
Age at intervention, years*	median(IQR)	3.1(1.1–6.8)	3.6(1.2–7.6)	3.0(0.7-6.1)	.74
PM, yes	n (%)	2(9)	2(15)	0(0)	.19
Cardiovascular medication, yes	n (%)	10(44)	5(39)	5 (50)	.58
ACE/ARB	n (%)	6(26)	4(31)	2(20)	.56
Beta-blockers	n (%)	2(9)	1(8)	1(10)	.85
Diuretics	n (%)	2(9)	1(8)	1(10)	.85
Warfarin	n (%)	5(22)	3(23)	2(20)	.86
Aspirin	n (%)	3(13)	2(15)	1(10)	.70

Abbreviations: ACE, angiotensin converting enzyme; ARB, angiotensin receptor-2 blockers; AV, atrioventricular; ccTGA, congenitally corrected transposition of the great arteries; d-TGA, dextro-transposition of the great arteries; F, female; IQR, interquartile range; M, male; n, number; PA, pulmonary atresia; PM, pacemaker; TCPC, total cavo-pulmonary connection; ToF, tetralogy of Fallot.
*Age at TCPC surgery or correction or ToF. Presented *P* values represent comparison between intervention group and controls. Mann-Whitney *U* test was applied in comparison of age and age at intervention; in all other comparisons chi-square or Student's *t* test was used.

weight and peak O_2 pulse. However, in comparison between the intervention group and control group no differences were found regarding absolute peak VO_2 (ml/min) or peak VO_2 indexed to body weight (ml/kg/min) (285[−200 to 535] ml/min vs 17[−380 to 306] ml/min, $P = .10$) (3.6[−2.6 to 6.4] ml/kg/min vs 0.6[−3.5 to 4.9] ml/kg/min, $P = .12$). Furthermore, the increase in peak O_2 pulse did not differ between the groups (1.3[−1.7 to 4.2] ml/heartbeat vs 0.4[−1.2 to 2.4], $P = .21$ (Table 2, Figure 1A–D).

3.2 | EQ-VAS, HADS, and ESE

No differences were found within or between groups preintervention and postintervention regarding self-reported QoL, prevalence of anxiety and depression or exercise self-efficacy (Table 3).

3.3 | Compliance

Compliance to exercise training protocol, defined as the number of completed training sessions in relation to the possible number of sessions, was in mean 79% ± 17 (median 83%, 47%–100%). The number of registered exercise occasions ranged from 17 to 36 of 36 possible occasions.

3.4 | Adverse event

In one case, the exercise training was discontinued due to the patient experiencing discomfort and possible arrhythmia during a session of exercise training. No arrhythmia was detected on a subsequent exercise test or at Holter registration. No other adverse events occurred.

TABLE 2 Preintervention, postintervention, and change in cardiopulmonary exercise test data in intervention group vs control group

	Preintervention			Postintervention			Change after intervention		
	Intervention group	Control group	*P*	Intervention group	Control group	*P*	Intervention group	Control group	*P*
CPET incremental									
VO_2 peak, ml/min	1865 (1191–2355)	1601 (1215–2650)	.74	1870 (1040–2642)	1688 (1326–2367)	.26	285 (−200 to 535)	17 (−380 to 306)	.10
VO_2 peak, ml/kg/min	23.4 (14.8–29.4)	23.6 (18.1–28.1)	.98	26.9 (13.0–33.6)	24.8 (18.1–28.4)	.23	3.6 (−2.6 to 6.4)	0.6 (−3.5 to 4.9)	.12
Peak O_2 pulse, ml/heartbeat	10.3 (7.3–13.7)	9.5 (6.8–15.1)	.99	12.0 (8.3–15.0)	10.8 (8.2–14.0)	.48	1.3 (−1.7 to 8.5)	0.4 (−1.2 to 2.4)	.21
Peak workload, W	155 (100–220)	150 (110–200)	.69	170 (90–240)	140 (110–200)	.07	20 (−10 to 70)	0 (−20 to 15)	**.003**
RER	1.19 (0.99-1.51)	1.22 (1.02-1.36)	.61	1.20 (1.13-1.40)	1.20 (0.98-1.29)	.52			
Constant work rate at 75% of peak workload:									
Test duration *min*	14 (4–33)	9 (3–20)	.11	28 (8–68)	9 (5–16)	**.001**	12 (−4 to 52)	0 (−4 to 5)	**.001**

Abbreviations: CPET, cardiopulmonary exercise test; RER, respiratory exchange ratio.
Data are presented as median (range). Bold text indicates a *P* value $< .05$.

4 | DISCUSSION

This is the first study to evaluate endurance capacity in addition to peak aerobic capacity after exercise training in adults with complex CHD. The present study shows that home-based high intensity interval training on a cycle ergometer has a great impact on endurance capacity as well as on maximum exercise capacity in adults with complex CHD.

4.1 | Exercise capacity

Peak VO_2 (ml/min) increased within the intervention group but not in comparison to the control group. However, the peak work rate for the intervention group increased in comparison to the control group which altogether indicates an improvement in peak aerobic capacity. The increase in peak VO_2 in previous studies was approximately 8%,[14,15,18] and in the present study the corresponding increase within the intervention group was 15%. An increase in aerobic capacity could be of significance in daily activities. In patients with complex congenital heart lesions, especially with impaired NYHA class, activities of daily living might be in line with or even exceed their individual exercise capacity.[5] In these cases, an exercise training induced improvement of exercise capacity could play an important role in coping with activities of daily living. In adults with complex CHD, the central adaption to exercise training is usually blunted,[36,37] which might lead peripheral mechanisms, that is, increased muscle capillarization and oxidative capacity, to play an even greater role in the response to exercise training.[38] The important increase in endurance capacity may actually reflect this mechanism. It is noteworthy that modest increases in peak VO_2 (ml/min) and peak work rate after exercise training corresponded to a substantial increase in time duration at constant work rate CPET; this result was previously reported in patients with COPD.[28,39] Our results imply that endurance capacity might be a more clinically relevant measure of change in exercise capacity after exercise training in adults with complex CHD.

4.2 | Exercise testing

Peak VO_2 derived from incremental CPET is frequently used and often considered the "gold standard" measure of peak aerobic exercise capacity.[25,26] When assessing the peak aerobic exercise capacity, it is important that the test is performed with maximum effort. The RER $\geq$ 1.10 is considered as a measure of maximum effort being reached.[25] In the present study, this limit was reached by the majority of the participants (Table 2). However, in adults with complex CHD difficulties in reaching this limit was previously reported.[6,40] This phenomenon was to some extent also observed in our population. Pulmonary limitation of the exercise capacity has been proposed to cause this limited ability to reach RER $\geq$1.10.[25] Recently, submaximal outcome measures calculated from the incremental CPET, that is, ventilatory anaerobic threshold (VAT), oxygen uptake efficiency slope (OUES), and VE/VCO_2 slope, have emerged as useful in evaluation of exercise capacity and as prognostic tools. Furthermore, these parameters do not require a test performed with maximum effort.[26,40,41] In our study, we

TABLE 3 Preintervention, postintervention and change in data regarding self-reported prevalence of anxiety and depression (HADS), quality of life (EQ5D VAS), and exercise self-efficacy (ESE)

	Preintervention			Postintervention			Change after intervention		
	Intervention group	Control group	*P*	Intervention group	Control group	*P*	Intervention group	Control group	*P*
HADS Anxiety	4(1–9)	4(0–7)	.69	5(2–9)	6(0–8)	.72	1(−3 to 3)	1(0–3)	.28
HADS Depression	2(0–9)	2(0–5)	.26	2(0–5)	2(0–6)	.97	0(−4 to 2)	0(−1 to 4)	.18
EQ-VAS	77.5(35.0–99.0)	89.5(70.0–99.0)	.10	78.8(48.0–99.0)	85.5(35.0–99.0)	.31	0(−21.0 to 25.0)	0(−55.0 to 9.0)	.42
ESE	32(16–39)	30(15–40)	.88	28(11–40)	29(18–40)	.67	−5(−12 to 8)	−1(−6 to 6)	.23

Abbreviations: EQ-VAS, EuroQol Vertical Visual Analogue Scale; ESE, Exercise Self-Efficacy Scale; HADS, Hospital and Anxiety and Depression scale. Data are presented as median (range).

took this a step further and used a submaximal exercise test in addition to the incremental CPET and found a substantially larger (median change 12 min, 89%) increase in submaximal exercise capacity in comparison to peak VO_2 (15%). With reference to the patients' performance capacity in daily activities, increased endurance might better illustrate the benefits of improved aerobic capacity and thereby be a more clinically relevant measure. The increase in endurance capacity we found is in line with previous studies in patients with COPD. Porszasz et al.[39] reported a mean increase of 11.6 ± 8.1 minutes in duration at constant work rate CPET after exercise training, while Cambach et al.[42] reported a mean increase of approximately 7 minutes in duration. An increase of 1.6–3.3 minutes has been suggested as a minimal clinically important difference in response to exercise training in patients with COPD.[43,44] In our intervention group, all patients except one increased the time duration at constant work rate CPET above this suggested level of minimal clinical importance. This particular patient did not comply fully with the exercise training protocol fulfilling only 17 of 36 (47%) of the possible exercise training sessions.

4.3 | Exercise training protocol

As stated in the current recommendations on physical activity and recreational sports in adults with CHD, exercise prescriptions should be individualized.[11] We aimed to provide the patients in the intervention group with an individually adjusted exercise training protocol based on the results of the cardiopulmonary exercise tests. Different modes of exercise training, for example, walking, interval training with step aerobics, and moderate continuous training on a cycle ergometer have been used in previous studies.[17,18,23,24] The present study is the first to use home-based moderate to high intensity interval exercise training on a cycle ergometer in a population of adults with different complex congenital heart lesions. Studies in adults with systemic right ventricle have shown that home-based exercise training is safe, feasible and effective with regard to exercise capacity without negative effects on the systemic right ventricle.[17,18,24] In patients with heart failure, interval training was reported to improve exercise capacity more than a moderate continuous exercise training mode.[22] The present study

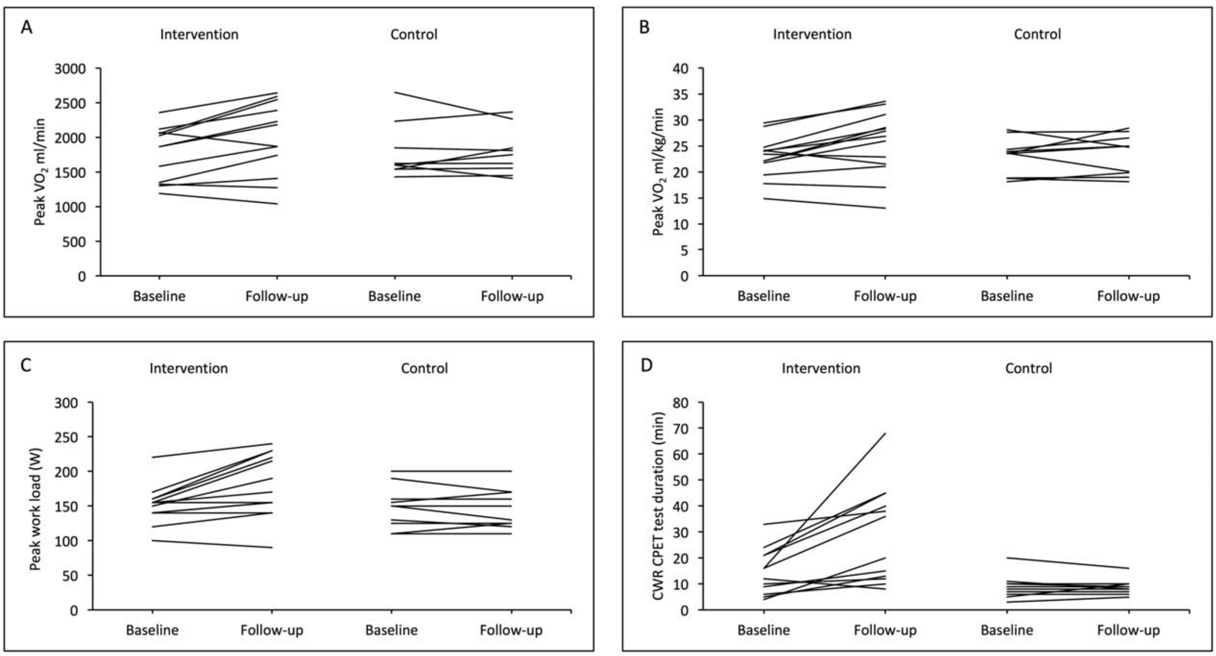

FIGURE 1 A-D, Individual cardiopulmonary exercise test data at baseline, at 12-week follow-up and change from baseline to follow-up in intervention group

showed that home-based interval exercise training increased endurance capacity as well as peak aerobic exercise capacity in adults with complex congenital heart lesions. The finding of markedly increased endurance capacity, in addition to peak capacity, contributes important information to previous exercise training studies in this population.

4.4 | Quality of life

In CHD, self-reported quality of life is known to be associated with physical activity level.[45] Here, we report that self-reported quality of life remained unchanged after intervention which is in line with results previously shown by others.[15] In contrast, positive effects of exercise on quality of life has been reported.[23] The population in the present study rated their quality of life as rather high preintervention which might explain the unchanged results.

4.5 | Compliance

As many patients with complex heart lesions are in the "middle of life" and occupied with studies, work, children, and family activities, a home-based exercise training protocol was chosen to improve adherence to study protocol. In addition, participants were contacted by phone every week, which probably also contributed to compliance. The mean compliance in the present study (79%) was in line with previously presented results (68%-77%).[14,17,18]

4.6 | Limitations

As in previously presented studies on exercise training in adults with CHD, our study population was rather small which somewhat limits the generalizability of the results. However, the results are in line with previous studies which further strengthen exercise training as a part of the rehabilitation of adults with complex CHD. Furthermore, our study population consisted of patients with different complex diagnoses that to a greater extent reflect the diversity seen in the clinic, thus enhancing the generalizability.

This study was performed at two centers. The center recruiting 5 patients (22%) was not able to keep the investigators performing the exercise tests strictly blinded for group allocation. However, there was a prespecified protocol that was strictly followed in both centers. Furthermore, the same center had a different recruitment strategy that possibly could involve patients with more frequent clinical visits and thus potentially patients with more complex lesions. However, the numbers are small and the two patients performing the exercise protocol did not obviously differ from the rest of the study population.

One concern of the constant work rate CPET that has been discussed previously in patients with COPD is the power/duration relationship.[28] This means that the endurance time varies depending on the workload (power) used during the test. However, there is no consensus on optimal power to use which complicates comparison of results between studies. To standardize, we used 75% of peak work rate that was used previously in COPD patients.[39,42]

4.7 | Conclusions

Home-based interval exercise training increased the endurance capacity at 75% of peak work load by 12 minutes as well as peak exercise capacity in adults with different complex congenital heart lesions. Substantially increased endurance capacity in the spectrum of daily activities is what most patients need. Therefore, endurance capacity might be a more clinically relevant target than solely peak oxygen uptake in patients with complex congenital heart lesions.

ACKNOWLEDGMENT

We are grateful to the personnel at the department of Clinical Physiology at the Heart Center, Umeå University Hospital who conducted the exercise tests and to the staff at the GUCH-center in Göteborg.

CLINICAL TRIAL REGISTRATION

ClinicalTrials.gov, identification:NCT01671566

CONFLICT OF INTEREST

None

AUTHOR CONTRIBUTIONS

All authors read and approved the final version of the manuscript.
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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

FIGURE S1 Example of the interval exercise training protocol. The exercise training session had an initial 8 min warm-up without load or with very low load. During the first two weeks, the protocol consisted of three intervals and thereafter four intervals. The work load during each interval was adjusted by the patient to reach the individual training heart rate. The patients were also instructed to reach a perceived exertion corresponding to 14-16 on the Borg scale. The intervals were separated by an active recovery periods of 3 minutes without load or with very low load. Each session ended with a cool down period of approximately 5 min

How to cite this article: Sandberg C, Hedström M, Wadell K, et al. Home-based interval training increases endurance capacity in adults with complex congenital heart disease. *Congenital Heart Disease*. 2018;13:254–262. https://doi.org/10.1111/chd.12562