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RESEARCH LETTER

Cellphone application rehabilitation management and evaluations of cardiopulmonary function and motor development in infants with congenital heart disease: a pilot study

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Congenital heart disease (CHD) has an estimated prevalence of 0.9%, with 0.3% requiring interventional or surgical intervention very early in life. Currently, CHD surgery tends to be performed at a younger age. The continued management of the condition is dependent on postoperative care and rehabilitation since the success rate of surgery has significantly increased [1, 2]. According to American Heart Association guidelines published in 2012, primary care providers were encouraged to refer CHD children who had undergone cardiac surgery for early developmental evaluation and intervention [3]. At present, the majority of these programs are designed for children who are preschool or school-aged, and infants with CHD who have undergone surgery but do not yet have access to a standardized cardiac rehabilitation (CR) program; additionally, postoperative CR and evaluation indexes of cardiac function and motor development in the infant population are still unexplored [4]. Infant are not fully developed in the cardiopulmonary system and lack the ability to cooperate, making them ineligible for traditional rehabilitation activities and cardiopulmonary function assessments. We introduced online cellphone application (APP) remote management into our study, and designed a suitable exercise program, as well as guidance for parents according to the developmental level of different children, because most rehabilitation tasks need to be completed at home [5].

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In a pilot study, we aimed to verify the feasibility, safety, and efficacy of this trial, which concentrated on three areas: the viability of home-based APP management, exercise with specific intensity that can be performed by the infant-age group, other evaluation indexes representing cardiopulmonary endurance, and the motor development assessment scale, which could be applied in the infant group.

We estimated their cardiopulmonary capacity by evaluating the left ventricular ejection fraction (LVEF) and heart rate (HR) fluctuation. The rate of increase in HR (rHRI) and rate of recovery in HR (rHRR) are significantly correlated with maximal oxygen uptake (VO_2max), a crucial metric for evaluating cardiopulmonary endurance [6, 7], especially demonstrating that postexercise heart rate recovery is directly determined by exercise cardiac reserve [8, 9]. Alberta and Checklist of neuro-intellectual development 0–6 years were applied in this study, and higher Alberta scores are longitudinally related to more advanced activities and personal-social competencies [10]. The Alberta scale can comprehensively assess neuromotor development in infants, with not only good compliance but also high sensitivity and specificity, allowing for the timely identification of children at developmental delay [11, 12]. We hypothesized that regular exercise can enhance both motor abilities and cardiovascular endurance in infant patients.

Home-based rehabilitation of CHD patients was a randomized controlled trial conducted at Beijing Children's Hospital in 2021–2022 for evaluating the prognosis of growth development and cardiopulmonary function in infants with CHD (aged 4–8 months) with atrial septum defects (ASDs) or ventricular septum defects (VSDs). Patients with chromosomal abnormalities and a family history of mental retardation, small for gestational age and prematurity, a history of perinatal asphyxia and hyperbilirubinemia, and a history of central nervous system disease or imaging suggestive of brain dysplasia were excluded. This pilot study protocol was approved by Capital Medical University and Beijing Children's Hospital. All study volunteers provided written informed consent. This study was registered in ClinicalTrials.gov (NCT05518136).

Eligible participants were randomized by a 1:1 allocation ratio by computer either to the recovery group or control group. Upon initial enrollment, weight, height, body mass index (BMI), and LVEF were measured, and developmental evaluation was conducted in both groups before surgery. We recorded their Alberta and developmental quotient (DQ), including five scale zones, and changes in real-time HR during tests. Specifically, resting HR and HR at 1, 3, 5, and 10 minutes (Max HR) during exercise were captured and HR at 3, 5, and 7 minutes after the assessment test were recorded. By simplifying the HR data, we calculated their rHRI at 3, 5, and 10 minutes and their rHRR at 3, 5, and 7 minutes after exercise and defined the mean value as their final indicators [13]: $rHRI_{(x)min} = (HR_{xmin} - HR_{resting})/X$; $rHRR_{(x)min} = (HR_{Max} - HR_{xmin})/X$. In contrast to rHRR, rHRI is negatively correlated with VO_2max. A fast rHRI and slow rHRR represent poor aerobic endurance [13]. All assessments were repeated at 1, 3 and 6 months after the surgery.

LVEF was recorded according to preoperative cardiac ultrasound results. The Alberta test and Neuro-intelligence Scale were performed by doctors from the healthcare department before surgery. While exercising, the patients' resting HR, rHRI and rHRR were monitored by a wearable device in real time. For the recovery group, parents were told to keep this device to connect with our Rehabilitation Management APP "TongXin" (Supplementary Fig. 1) on their cellphones, signed up and created a file for their children. This application, which was developed by Wenxin Technology,

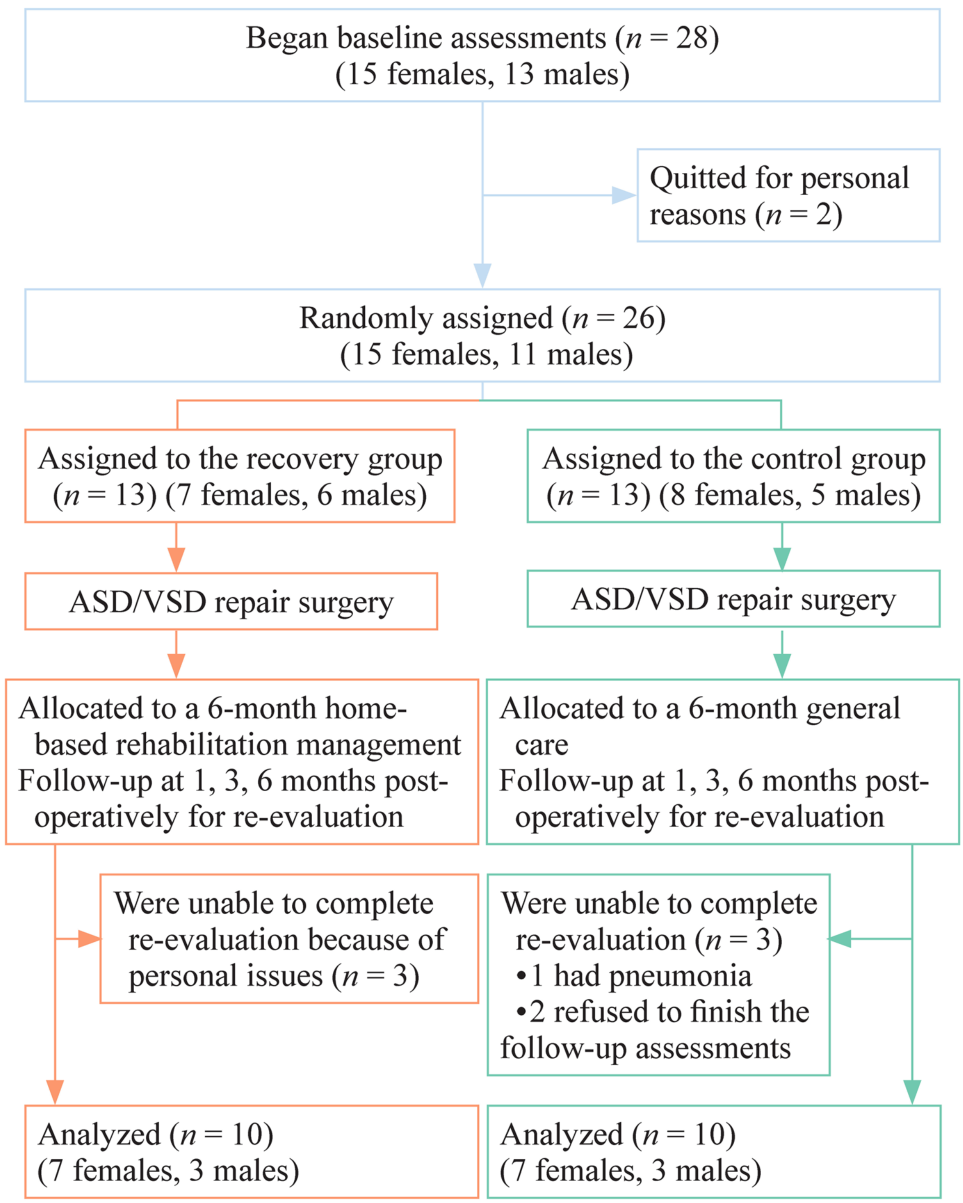

Fig. 1 Flow diagram of study participants. Consolidated Standards of Reporting Trials (CONSORT) diagram shows the flow of patients through the study. *ASD* atrial septum defect, *VSD* ventricular septum defect

Table 1 Baseline characteristics

Variables	Control group *(n = 13)*	Recovery group (*n* = 13)
Age, mon	3.8 (1.61)	4.4 (1.96)
Gender		
Female	8 (62%)	7 (54%)
Male	5 (38%)	6 (46%)
Type of CHD		
ASD	3 (23%)	4 (31%)
VSD	10 (77%)	9 (69%)
Height, cm	67.2 (5.01)	68.1 (4.20)
Baseline weight, kg	6.9 (1.69)	7.3 (1.39)
Baseline BMI, kg/m^2	15.10 (1.76)	16.0 (2.06)
Baseline LVEF, %	72.2% (0.04)	66.2% (0.05)
Resting HR, bpm	133.4 (5.62)	136.1 (6.82)
Max HR, bpm	164.8 (12.19)	166.1 (10.08)
rHRI, beat/min^2		
3 min rHRI	5.1 (3.00)	4.6 (2.09)
5 min rHRI	4.7 (2.76)	4.2 (1.44)
10 min rHRI	3.1 (1.33)	3.0 (0.71)
Mean rHRI	4.3 (2.30)	3.9 (1.26)
rHRR, beat/min^2		
3 min rHRR	4.1 (1.92)	4.2 (1.94)
5 min rHRR	3.9 (1.64)	3.6 (1.35)
7 min rHRR	3.6 (1.50)	3.5 (1.07)
Mean rHRR	3.9 (1.56)	3.8 (1.39)
Alberta score	24.0 (11.27)	27.8 (11.83)
Developmental quotient	81.3 (9.07)	82.5 (10.58)
Gross motor	78.0 (15.90)	77.6 (13.79)
Fine motor	81.9 (8.78)	79.6 (13.95)
Adaptability	83.0 (9.99)	83.3 (16.76)
Language	80.7 (11.49)	80.6 (16.93)
Social behavior	82.8 (11.54)	89.7 (11.39)

CHD congenital heart disease, *HR* heart rate, *ASD* atrial septum defect, *VSD* ventricular septum defect, *LVEF* left ventricular ejection fraction, *rHRI* rate of increase in heart rate, *rHRR* rate of recovery in heart rate

provided a platform for two-way feedback between patients and physicians. The "TongXin" app comprises a database that stores patients' basic information, clinical measures, and cardiopulmonary exercise test results. Moreover, it also contains exercise rehabilitation instructions, which are customized to cater to different rehabilitation stages of 1, 3, and 6 months postoperatively. The main menu consists of rehabilitation science, feeding advice for parents, rehabilitation exercise guidance, questionnaires and vaccination advice. The heart rate is recorded by a wearable device, which is worn during each exercise session. If a child's heart rate exceeds a target predetermined threshold, the system will remind their parents via the connected cell phone to stop exercising. In addition, the cardiac ultrasound re-evaluation outcomes and development assessment score are included in the profile of each child. One month after surgery, there were no specific training plans for all patients. Different training regimens were created for each patient in the recovery group between 1–3 months and 3–6 months following the procedure in accordance with the findings of the developmental evaluation and cardiac ultrasound. Parents were told to assist their children with certain exercises and complete a set amount of training time. Adverse events such as sweating, cyanosis and dyspnea were noted. Training motions included sitting balance, hand support, crawling and squatting training [14–16] and were scheduled for 1–3 months postoperatively; moreover, climbing over obstacles was scheduled for 3–6 months. The primary endpoint was defined as the baseline-to-6-month difference in cardiopulmonary capacity and physical fitness between the recovery and control groups. Student's *t* and Wilcoxon tests were used to evaluate between-group differences with respect to baseline characteristics. A *P* value of 0.05 was considered significant for all tests. Repeated measures analysis of covariance (ANCOVA) was applied with change from baseline as the dependent variable and recovery intervention, time, and rehabilitation multiplied by time interaction as independent variables. Moreover, the Spearman test was also applied to determine the correlations between LVEF and rHRI and rHRR. All analyses were performed using the R language (Version 3.6.3).

Between April 10, 2021 and December 28, 2021, participants were randomly assigned, with the final study visit on May 25, 2022. Of the 28 patients who agreed to participate, the study procedure excluded 2 (7%) due to refusal to cooperate for private reasons. Of the 26 participants who were randomly assigned and started the intervention after baseline assessments, 13 (50%) were assigned in the home-based rehabilitation group and 13 (50%) in the control group till the completion of the study. The Consolidated Standards of Reporting Trials (CONSORT) diagram for enrolled participants is summarized in Fig. 1. A total of 28 patients (13 females, 15 males) signed informed consent for screening, and 2 patients quit for personal reasons. Only 26 of them were assigned to baseline assessments (13 males, 13 females) and were randomly allocated to the recovery group (6 females, 7 males) and control group (7 females, 6 males) at a ratio of 1:1. Three patients in the recovery group were unable to return to our hospital during the follow-up phase for a postoperative re-evaluation. One patient in the control group was readmitted to the hospital due to pneumonia, and two patients refused to complete the follow-up assessment. Only 10 patients in each group finished the 6-month project.

Table 1 presents the baseline characteristics of 26 participants, showing no differences in LVEF ($P > 0.05$), rHRI and rHRR as well as Alberta score and DQ between the two groups. The DQ results mainly include gross motor,

Table 2 Changes in LVEF and heart rate fluctuation

Variables	Control group ($n=10$)	Recovery group ($n=10$)	Between-group *P* value
LVEF, %			
Baseline	72.2% (0.01)	66.2% (0.01)	0.007
Change at PO 1 mon	− 1.2 (1.07)	− 0.2 (2.13)	0.680
Change at PO 3 mon	− 1.7 (1.07)	2.4 (1.77)	0.063
Change at PO 6 mon	4.2 (1.34)	5.5 (1.73)	0.002
Mean rHRI, beat/min^2			
Baseline	4.3 (0.73)	3.9 (0.40)	0.880
Change at PO 1 mon	− 0.52 (0.33)	− 0.59 (0.35)	0.893
Change at PO 3 mon	0.21 (0.34)	− 0.50 (0.70)	0.378
Change at PO 6 mon	− 0.47 (0.37)	− 1.21 (0.49)	0.241
Mean rHRR, beat/min^2			
Baseline	3.9 (0.50)	3.8 (0.44)	0.913
Change at PO 1 mon	0.63 (0.34)	− 0.07 (0.30)	0.137
Change at PO 3 mon	0.03 (0.54)	0.47 (0.30)	0.483
Change at PO 6 mon	− 0.13 (0.46)	1.45 (0.42)	0.020

LVEF left ventricular ejection fraction, *rHRI* rate of increase in heart rate, *rHRR* rate of recovery in heart rate, *PO* postoperative

fine motor, social behavior and adaptability scores. Rating and grading criteria: developmental quotient (DQ) = (average of five zones/age of actual months) × 100. DQ ≥ 130 is considered as exceptional, 120–129 as excellent, 110–119 as intelligent, 90–109 as moderate, 80–89 as delayed, 70–79 as marginal, < 70 as low, 50–69 as mildly low, 35–49 as moderately low, 20–34 as severely low, and < 20 as extremely severely low. The CHD patients enrolled in this study were mostly developmental delayed.

On the basis of follow-up records in Table 2, LVEF of the recovery group was elevated by a mean of 2.4% [standard error (SE) = 1.77; $P=0.063$] at 3 months and 5.5% (SE = 1.73; $P=0.002$) at 6 months; LVEF was also increased in the control group at 6 months by 4.2% (SE = 1.34) but showed a decrease of 1.2% at 1 month and 1.7% at 3 months postoperatively. The rHRI maintained a downward trend in the recovery group but declined by a mean of 0.59 beat/minute^2 (SE = 0.35; $P=0.893$) at 1 month after surgery. Changes between groups were not obvious, although at 6 months, rHRI in the recovery group had dropped by 1.21 beat/minute^2 (SE = 0.49; $P=0.241$). However, the rHRR of the recovery group was improved by a mean of 1.45 beat/minute^2 (SE = 0.42; $P=0.02$) at 6 months later, while it decreased by 0.13 beat/minute^2 (SE = 0.46) in the control group.

In this study, there were no significant differences between the two groups in terms of developmental levels prior to and following surgery. As shown in Table 3 and Fig. 2, the Alberta score for intelligence and motor skills was greatly elevated in the recovery group, with mean values of 30.9 (SE = 2.43; $P<0.001$) at 3 months and 47.7 (SE = 3.27; $P=0.001$) at 6 months; it was also higher in the control group at 6 months (31.7, SE = 2.66) postoperatively. The DQ score maintained an upward trend in both groups but improved by a mean of 3.1 (SE = 1.23; $P=0.576$) at 1 month after surgery in the recovery group and 16.5 (SE = 1.63; $P=0.001$) at 6 months. The within-group changes were obviously evident at 6 months. There was also a notable difference in fine motor skills scores. The recovery group had a mean increase of 18.0 (SE = 2.11; $P=0.001$) at 6 months, while the control group only showed an increase of 8.2 (SE = 1.02). However, the gross motor function of the recovery group was improved by a mean of 15.1 (SE = 2.51; $P=0.514$) at 6 months later compared to 17.7 (SE = 2.3) in the control group.

We collected LVEF, rHRI and rHRR of each patient in both groups at the same period before and after surgery for correlation analysis. Spearman's test was used to analyze the correlations between LVEF and rHRI and rHRR, and the results in Fig. 3 indicated that there were no significant correlations between LVEF and rHRI ($r=0.104$; $P>0.05$) or rHRR ($r=-0.075$; $P>0.05$).

During the 6-month follow-up period, there were no deaths or adverse feedback in either group, but one patient in the control group experienced a rehospitalization because of pneumonia two months after surgery. Adverse events may include paleness, sweating, wheezing, tachycardia, and other discomfort while exercising at home. The wearable device, which could record the real-time heart rates, was used as a safety monitoring tool, allowing parents and doctors to monitor it at any time and providing timely feedback to doctors via the Internet client.

Table 3 Changes in neuro-intelligence development and motor skills

Variables	Control group ($n=10$)	Recovery group ($n=10$)	Between-group P value
Alberta score			
Baseline	24.0 (3.57)	27.8 (3.74)	0.472
Change at PO 1 mon	5.3 (1.02)	4.1 (2.16)	0.622
Change at PO 3 mon	13.0 (1.73)	30.9 (2.43)	<0.001
Change at PO 6 mon	31.7 (2.66)	47.7 (3.27)	0.001
Developmental quotient (DQ)			
Baseline	81.3 (2.87)	82.5 (3.34)	0.788
Change at PO 1 mon	2.2 (0.99)	3.1 (1.23)	0.576
Change at PO 3 mon	5.6 (0.96)	10.7 (1.51)	0.010
Change at PO 6 mon	8.9 (1.05)	16.5 (1.63)	0.001
Gross motor skills score			
Baseline	78.0 (5.03)	77.6 (4.36)	0.953
Change at PO 1 mon	4.5 (1.93)	4.0 (1.97)	0.858
Change at PO 3 mon	11.1 (1.79)	10.7 (2.78)	0.905
Change at PO 6 mon	17.7 (2.30)	15.1 (2.51)	0.514
Fine motor skills score			
Baseline	81.9 (2.78)	79.6 (4.41)	0.850
Change at PO 1 mon	4.3 (1.10)	1.1 (1.42)	0.091
Change at PO 3 mon	6.6 (0.98)	9.1 (1.59)	0.197
Change at PO 6 mon	8.2 (1.02)	18.0 (2.11)	0.001

DQ developmental quotient

With the advent of sports rehabilitation medicine, it has been gradually accepted that exercise has more advantages for children with heart disease. Previous studies suggested that aerobic exercise enhancing lung function and alveolar oxygen supply are envisaged as thoracic mobility improvement. As a consequence, exercise performance may benefit from pulmonary vascular dilatation and a reduction in right ventricular afterload [17]. Exercising can also improve endothelial function and coronary circulation, likely by recruiting collateral vessels and possibly increasing blood flow in the myocardium [6]. Moderate exercise is known as a stimulator of NO release, which may improve endothelial and autonomic functions. This might result in a greater decrease in afterload, which in turn increases LVEF and stroke volume [18]. Considering this fact, regular physical exercise can be considered a protective factor of cardiopulmonary function [19]. Since the average life expectancy of a child born with CHD is now well into adulthood, it is crucial to take preventative measures early on to minimize the risk of developing complications in later life. Children who have had surgery will still suffer varying degrees of cardiac insufficiency, physical development and neuropsychological development delays during the rehabilitation process [20–22]. Even mild cardiac disease can lead to delays in the development of neural intelligence and motor ability in infants, and early rehabilitation exercise training in infants can improve such backwardness to a certain extent and eventually improve to the normal level of this age group [5, 23].

Currently, infants with CHD who have undergone surgery do not yet have access to standardized CR management, as the majority of these programs are geared for preschool- or school-aged children. In addition, many guidance and exercise evaluations are inappropriate for infants, which makes CR in this population a new field. Moreover, the emergence of COVID-19 has brought attention to the conveniences of home-based exercise intervention as a rehab modality. This has led to our preliminary studies assessing the effectiveness of home-based or remote CR strategies. In addition, it may also be a timely option for CHD patients to stay physically active, avoiding needless hospital travel [24]. From our perspective, this home-based exercise plan through APP would be a viable guidance for patients and improve the aerobic performance of CHD children compared to a thorough baseline assessment. Patients in the rehabilitation group were very cooperative with this form of online medical management; meanwhile, data from home training and feedback from parents can be better collected for upcoming adjustments to the rehabilitation plan.

As young CHD patients cannot finish a common exercise stress examination, the treadmill test, the key point of this research is selecting the appropriate indexes to reflect cardiopulmonary endurance and achievable exercise for infant patients. Previous researches indicated that rHRR and rHRI were significantly correlated with maximal oxygen uptake (VO_2max), which is an important indicator of cardiopulmonary endurance, demonstrating that heart rate fluctuation is determined by exercise cardiac reserve [8, 25]. In this study, however, we cannot assume that LVEF, rHRI and rHRR can fully reflect the level of cardiopulmonary endurance in infants; additionally, there were no correlations between LVEF and heart rate changes according to Fig. 3. From the perspective of rHRI and rHRR in Fig. 2, it cannot be stated that the recovery group is superior to the control group. Therefore, targeted rehabilitation training at home may take longer to verify the improvement in cardiopulmonary function [15].

On the other hand, infancy and early childhood are periods of rapid motor development, and the performances of

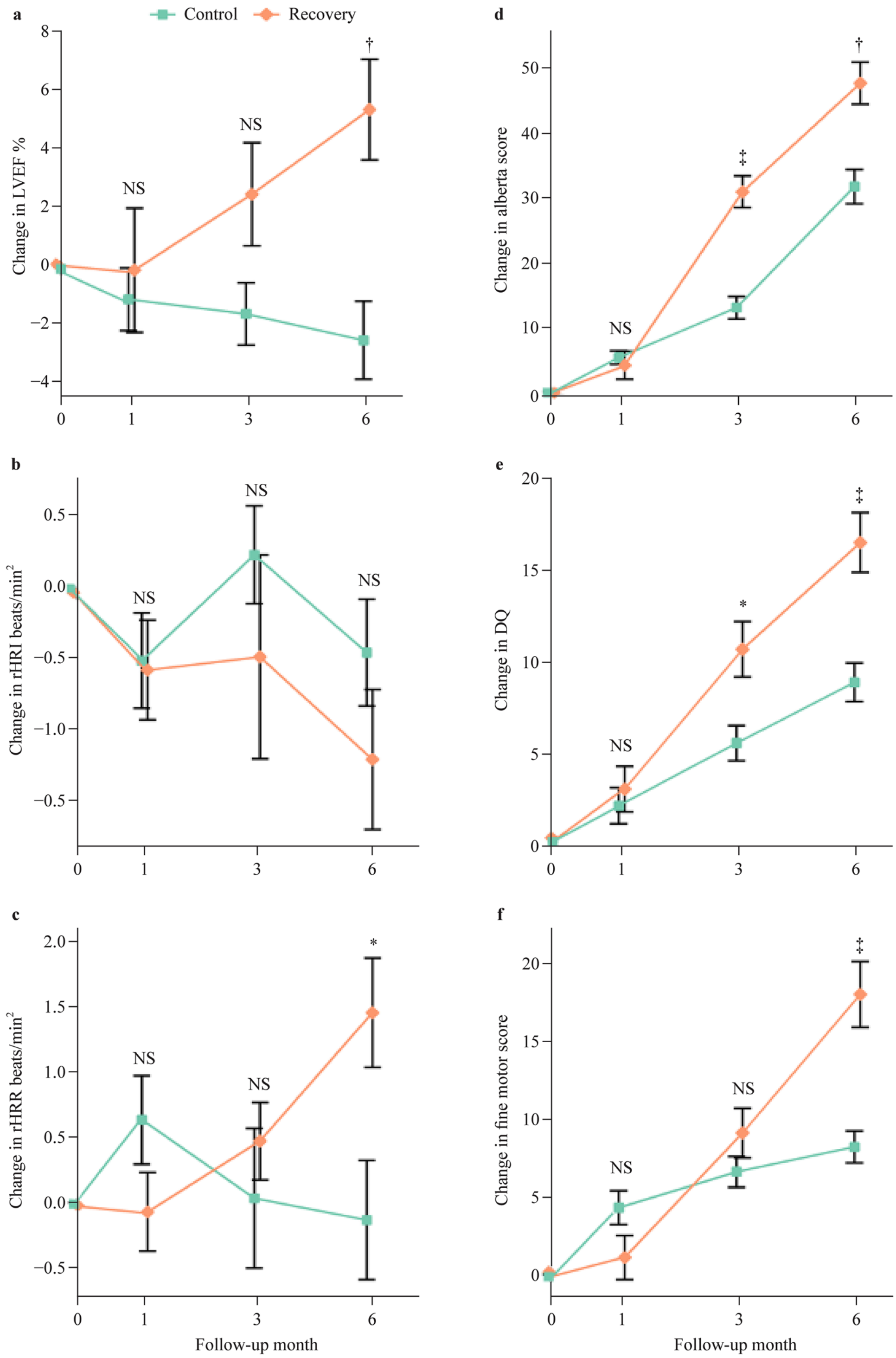

Fig. 2 Within-group changes (mean, SE) are shown for the cardiopulmonary endurance parameters of LVEF (**a**), rHRI **b** and rHRR **c**. The changes of neuro-intelligence and motor skills were illustrated, including Alberta score **d**, DQ **e** and fine motor score **f**. *ns*, $P \geq 0.05$, * $P < 0.05$, † $P < 0.01$, ‡ $P < 0.001$. *SE* standard error, *LVEF* left ventricular ejection fraction, *rHRI* rate of increase in heart rate, *rHRR* rate of recovery in heart rate, *DQ* developmental quotient

patients in different months are heterogeneous. Therefore, it is necessary to select a sensitive and specific scale for motor development assessment. The preoperative evaluation results of the above two groups of infants with simple CHD revealed that their development level was still behind that of normal infants of the same age, especially in motor ability, partly because of the loss of cardiopulmonary endurance and the developmental delay of the nervous system caused by abnormal hemodynamics [26]. A considerable improvement in cardiopulmonary endurance, as measured by heart rate variability, was observed in both groups after surgery (Fig. 2). The exercises we chose, such as crawling, climbing and squatting training, which target the greater lower extremity muscle, may help to pump augmented systemic

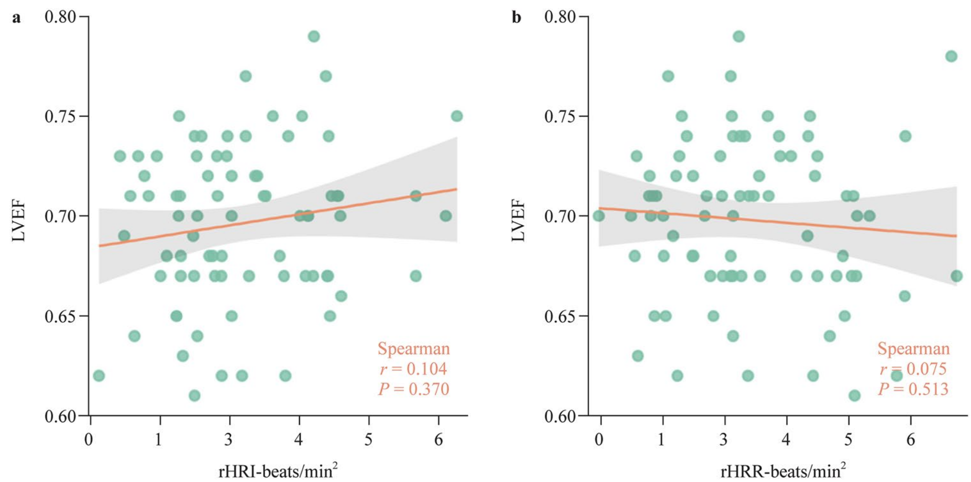

Fig. 3 Spearman's correlation analysis of LVEF and rHRI **a** $P=0.370$; LVEF and rHRR **b** $P=0.513$. *LVEF* left ventricular ejection fraction, *rHRI* rate of increase in heart rate, *rHRR* rate of recovery in heart rate

venous return at the initiation of exercise in upright individuals with normal cardiorespiratory circulation since peripheral muscle mass may be a surrogate for the systemic venous muscle pump [27, 28]. Meanwhile, children in the recovery group performed much better in reassessments of motor and intellectual development, and there was a statistically significant difference in fine motor skills.

According to this research and online feedback from parents, CR training can greatly enhance the athletic ability of children. General motor or even specific fine motor skills and neuro-intelligence development can both benefit from CR management. By promoting resiliency and measurable accomplishments, the goal needs to shift to meeting the patient at their current level of fitness, both physically and mentally. We hope that this pilot study will provide a better understanding of postoperative rehabilitation among CHD infants to apply online and offline synchronous management in a more comprehensive way.

The sample size in our study is relatively small. We were unable to include exactly the statistically required number of patients with CHD. This means that the current data are underpowered to detect effect sizes < 0.75 SD (statistical analysis section), and the test power and sensitivity were diminished, which we considered acceptable for this pilot study. Consequently, caution was needed in interpreting the results, which has limited the generalizability. However, this is the first randomized exercise training trial in infant CHD patients, and we feel that the data are available as primary guidance for child rehabilitation programs. According to power analysis and sample size (PASS) analysis, it is assumed that 80% of the patients in the rehabilitation group recovered better than those in the control group, and the statistical level is set at 0.05. Based on the preliminary experimental work, we defined the Alberta score, developmental quotient, and rHRR (heart rate recovery rate) as the main effects of this study. The mean and standard deviation of each indicator in both groups were calculated for the superiority test. Allowing for 10% attrition, we planned to recruit 88 participants in a future study.

In conclusion, this randomized controlled study provides preliminary data suggesting that LVEF and motor developmental level were elevated by 6-month home-based exercise training in infancy CHD patients. Moreover, home-based exercise can greatly help infants perform better in motor and intelligent development assessments, especially working on fine motor skills. Current research holds promise for the development of programs that are practical and scalable, and we sincerely hope to see their applications in most clinical sites soon.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s12519-023-00734-6.

Author contributions ZGJW: conceptualization, methodology, writing–original draft; LZQ: supervision, methodology; MY: investigation, project administration; ZYB and YDL: project administration; DN: supervision. YHL investigation; LSJ and ZJR: resources acquisition.

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Data availability We believe that the data from this trial will be more meaningful for the future research with a larger sample size. However, we are pleased to share it with people who need it or show great interest in this study. The datasets that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Conflict of interest No financial or non-financial benefits have been received or will be received from any party related directly or indirectly to the subject of this article.

Ethical approval Research study protocols were approved by patients and their parents. Parents provided written informed consent to participate and the proof of consent can be requested at any time. This study was approved by the Medical Ethics Committee of Beijing Children's Hospital (REC approval number: 2021-E-043-Y-001).

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