Cardiology in the Young

Impact of exercise training in patients after CHD surgery: a systematic review and meta-analysis of randomised controlled trials

Mengyuan He1, Qiang Wang2 and Wei Zhang2

1Clinical School of Thoracic, Tianjin Medical University, Tianjin, China and 2Tianjin Chest Hospital, Tianjin, China

Abstract

Background: The goal of this meta-analysis is to evaluate the effects of exercise training on long-term health and cardiorespiratory fitness in participants with CHD after surgery and to investigate the optimal type of exercise training for post-operative patients and how to improve adherence to it. Methods: We searched the Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, and Web of Science from the date of the inception of the database through August 2021. Results: Altogether, 1424 records were identified in the literature search. Studies evaluating outcomes between exercise training and usual care among post-operative patients with CHD were included. The assessed outcomes were quality of life and cardiorespiratory fitness. We analysed heterogeneity by using the I2 statistic and evaluated the quality of evidence. Conclusions: In conclusion, participation in a physical exercise training programme was safe and improved fitness in patients after surgery for CHD. We recommend that post-operative patients with CHD participate in physical exercise training. Additional research is needed to study the various forms of exercise training and their impact on quality of life.

In the current era, the proportion of children and adolescents with CHD surviving into adulthood has dramatically increased due to medical and surgical remarkable progress, which has resulted in patients after CHD surgery showing long-term morbidity as reflected by reduced health-related quality of life, cardiopulmonary fitness, and activity declined with age.

As we know, exercise training is an efficient way of improving aerobic capacity and pulmonary function in children and adolescents after the surgical procedure. And exercise is not only a way for assessment but also considered therapy for CHD post-operative patients. Moreover, the American Heart Association recognises that patients with CHDs should emphasise the importance of daily physical activity and decreasing sedentary behaviour as appropriate for the patient’s clinical status. Furthermore, children and adults are recommended to perform moderate to vigorous exercise for ≥60 minutes a day, even in patients with CHD after surgery by current public health guidelines.

Few studies have focused on the effects of physical activity interventions for people after surgery for CHD. However, these studies included small numbers of patients and had different conclusions, which made the exact effects of physical activity not sure. Additionally, a systematic review mainly focused on cardiorespiratory fitness and health-related quality of life, although people with CHD were included, which has no post-operative participants. Indeed, due to a lack of knowledge of the exercise training for people with CHD, specialist paediatric cardiac clinics’ physical activity recommendations are not adequately discussed. And to our knowledge, there were few systematic reviews and meta-analyses of randomised controlled trials that have discussed the optimal type of exercise training and how to improve adherence to exercise training in post-operative CHD patients thus far.

This study aimed to systematically review the published controlled trials to evaluate the effects of exercise training on long-term health and cardiorespiratory fitness in participants with CHD after surgery and to investigate the optimal type of exercise training for post-operative patients and how to improve adherence to it.
Eligibility studies of this report met all following criteria: (1) reported paediatric (5 to 18 years old) or adult populations (>18 years old) after surgery for CHD; (2) should be exercise training as the intervention; (3) were randomised controlled trials; (4) compared to standard/usual care in individuals after surgery for CHD.

The main outcomes of interest were long-term health quality, as the quality of life determined by the Short-Form 36 item [SF-36] health survey and CHD-TNO/AZL Adult Quality of Life [CHD-TAAQOL] questionnaire, and cardiorespiratory fitness measured by peak oxygen consumption (peak VO₂, ml/kg/min).

Information sources and search strategy

Two independent authors (M.Y He and W. Zhang) searched The MEDLINE (accessed through PubMed), EMBASE, the Cochrane Library, and Web of Science were searched on 14 August 2021 for relevant studies, using the same unique search algorithm for each database, which were published up to July 2021 without any language restrictions. Search terms using a controlled vocabulary (Mesh terms and entry terms for MEDLINE) included three parts: study design, participants, and interventions. Box 1 (Supplementary File) lists the Mesh and entry words that were utilised.

Study selection

Duplicate articles were removed in the first step. Two investigators (M.Y He and W. Zhang) independently screened titles and abstracts for inclusion from the remaining references. Full texts and results were then retrieved and separately reviewed by the same reviewers for eligibility according to inclusion and exclusion criteria. Disagreements can be settled by discussion or consulting with the third author (Q. Wang).

Data extraction and analysis

Two authors (M.Y. He and W. Zhang) developed a data extraction form independently and extracted data from published reports, taking into account the following study characteristics: participants, such as average age and gender, intervention description, such as sample size, frequency, intensity, duration, and follow-up time, and outcomes. Any further information was obtained from the original authors by e-mail.

Quality of meta-analysis evidence

The quality of evidence was independently evaluated by two researchers (M.Y He and W. Zhang) according to the Cochrane Risk of Bias tool, which includes selection bias, performance bias, detection bias, attrition bias, reporting bias, and other biases.20

Statistical assessment

All included studies were assessed using Review Manager Version 5.4 (Cochrane Collaboration) and Stata/MP version 16.0. The I² test was used to assess the degree of heterogeneity among the results, with values ≥50% indicating significant heterogeneity. Fixed effects models were employed for no or low heterogeneity, whereas random-effects models were used for moderate and high heterogeneity. Continuous data were analysed as mean differences and 95% confidence intervals (CIs), as well as forest plots. In several studies, where data were reported as medians and interquartile ranges, we replaced them with means and standard deviations according to validated equations.21,22 To assess the contribution of individual studies to the degree of heterogeneity, a sensitivity analysis was performed, which comprised generating the meta-analysis estimate after excluding one study at a time. Egger’s regression asymmetry test and a funnel plot were used to evaluate publication bias. A p-value <0.05 was deemed statistically significant.

Results

Characteristics of population

1424 abstracts were identified after the initial search, from which 67 were considered as possibly relevant and retrieved for full text assessed according to eligibility criteria. We have shown the PRISMA flow diagram of studies in Figure S1.

This study contained just 8 randomised controlled trials10,12-17,23 with a total of 371 participants, including both genders. Correction of tetralogy of Fallot, Fontan circulation, and atrial switch technique or a systemic right ventricle for transposition of the great arteries were all included in the CHD surgical research. And Tetralogy of Fallot, Fontan, and transposition of the great arteries are the most common kinds of CHD. Table 1 shows that the samples in the final 8 papers ranged from 17 to 93, with a mean age of 13 to 40.1 years. The participants in three randomised controlled trials were adolescents and youngsters, whereas the participants in the other five randomised controlled trials were adults.

Exercise training

The information on exercise training for included studies was pooled into Tables 1 and 2.

Type and intensity

There were several sorts of exercise training, but they mostly engaged in aerobic exercise training at home, which primarily consisted of cycling and brisk walking. And peak VO₂ and heart rate, which were monitored using a heart rate monitor, were the primary determinants of their intensity. Only one randomised controlled trial25 combined aerobic and resistance training, to investigate its effects on the performance and oxygenation of peripheral muscular measured by utilising maximal voluntary contraction, limited time at 50% maximal voluntary contraction, the half time of recovery, and the recovery speed to maximal oxygenation.

Duration

The majority of the included randomised controlled trials had a 12-week follow-up period. One of the studies12 lasted 10 weeks, while another lasted 24 weeks.13 Patients of all included randomised controlled trials were followed up right away after the training programme. Training occurred 1–3 times each week, with the most occurring three times per week. Each training session lasted anywhere from 10 to 60 minutes. In one randomised controlled trials, the duration and frequency of the intervention, which was separated into three stages, steadily increased over time.13

Supervision and compliance

There were three experiments under the supervision of the instructor and two of them reported a high similarly attendance rate, which was 89%. Three studies with no supervision and only one of them showed a compliance rate of 67.7%. The percentage of expected training units determined from the patient’s training regimen was used to calculate training compliance. One of the
randomised controlled trials involved hospital and home aerobic exercise sessions, with a supervised exercise programme in the hospital and a 73% adherence rate. Patients were often reached via phone calls or e-mails from researchers to ensure adherence to the training.

Recruitment and death event

The recruiting data were presented in six of the nine papers, with participation rates ranging from 26% to 48.29%. The time-consuming nature of the research, according to Duppen et al,15 was the major reason for not participating. The drop-out rate was shown in 7 out of 8 publications, ranging from 0% to 28.57%. Personal, job-related, and experiment itself (rejections of second examination and training programme) factors were among them. There were no adverse events discovered. During the experimental period, both Westhoff-Bleck et al13 and Therrien et al10 found non-malignant arrhythmias during the experimental period. There was no need for intervention in any of these incidents and they were unrelated to exercise training.

Outcome results

Quality of life

Three studies used validated questionnaires to measure the quality of life.12,14,17 We did not undertake sensitivity analyses since there was no heterogeneity in the quality of life and peak VO2 between the exercise and control groups.

Subgroup meta-regression analysis

We ran a subgroup analysis of peak VO2 and found no significant difference both the training duration of 12 weeks (mean difference = 1.95[95%CI –0.50 to 44.40], I² = 0%, n = 161) and patients of repaired TOF only (mean difference = 1.90[95%CI –1.02 to 4.83], I² = 0%, n = 113, as illustrated in Figure S3).

Publication bias

Publication bias of including randomised controlled trials was evaluated by Egger’s test and graphed with funnel plots as shown in Figure S4. There was no evidence of publication bias for peak VO2 in the present study (p = 0.804).

Risk of bias

The risk of bias in outcomes across all studies was low or unclear located in Figure S5. However, three studies had a high risk of bias in allocation concealment (selection bias) because of non-blinded allocation17 and recruitment significantly depended on patients’ willingness10,12 though all included studies were randomised clinical trial studies. Furthermore, the authors reported poorly the details regarding whether participants and personnel were blinded and information regarding whether investigators were blinded, which resulted in unclear biases in performance and detection.

Discussion

The main result of this systematic review and meta-analysis shows that peak VO2 was increased after exercise training for post-operative patients with CHD when compared to usual care and it was certainly safe for these patients. However, there were little
| Study (Author, Y) | Intervention                                                   | Modality                                               | Intensity                                                   | Duration of each session | Follow-up time | Frequency (*per week) | Supervision        | Drop-out | Compliance |
|------------------|----------------------------------------------------------------|--------------------------------------------------------|-------------------------------------------------------------|--------------------------|-----------------|-----------------------|--------------------|----------|------------|
| Therrien, 2003   | Aerobic and home-based exercise programme                      | Cycling and brisk walking                              | 60 to 85% of baseline peak VO2/maximal HR                   | 50 min/30 min            | 12 weeks        | 3                     | Supervised/unsupervised | 22.22%   | 73%        |
| Dufler, 2014     | Aerobic exercise programme                                     | Brisk walking /jogging/running/bicycle/dynamic play    | 60–70% HR resting                                          | 60 min                   | 12 weeks        | 3                     | Yes                | 28.57%   | 89%        |
| Westhoff-Bleck, 2013 | Aerobic exercise training                                    | Cycling                                                | HR corresponds to 50% of peak oxygen uptake                | Phase I: 10/15 min       | 24 weeks        | Phase I (3)           | No                 | 20.8%    | 67.7%      |
| Duppen, 2015a    | The standardised aerobic exercise training programme            | Brisk walking /jogging/running/bicycle exercises/dynamic play | 60–70% HR resting                                         | 60 min                   | 12 weeks        | 3                     | Yes                | 3.2%     | 89%        |
| Duppen, 2015b    | Home-based aerobic consecutive exercise training programme     | Step aerobics                                           | 75–90% of maximal heart rate                              | 42 min                   | 10 weeks        | 3                     | No                 | 14.29%   | NP         |
| Novakovic, 2018a | High-interval training programme                              | Cycling or speed walking                                | 80% of HR peak in high-intensity exercise                 | 42 min                   | 12 weeks        | 2–3                   | NP                 | NP       | 92.90%     |
| Novakovic, 2018b | The moderate continuous training programme                     | Cycling or speed walking                                | 70% of HR peak in continuous intensity                    | 42 min                   | 12 weeks        | 2–3                   | NP                 | NP       | 89.20%     |
| Moalla, 2012     | Home-based aerobic cycling training                            | Cycling                                                | HR equal VAT                                               | 60 min                   | 12 weeks        | 3                     | No                 | 0        | NP         |
| Avilla, 2016     | combined aerobic and resistance training                      | Combined dynamic and resistance training                | 70%–80% of maximal HR                                      | 60 min                   | 12 weeks        | 1–2                   | Yes                | 0        | NP         |

Peak VO2: peak oxygen consumption; HR: heart rate; NP: not reported; VAT: ventilatory anaerobic threshold. The drop-out rate is just for the intervention group.
The maximal measure of CRF is one of the strong independent predictors of hospitalisation and morbidity. In the current study, maximal cardiorespiratory fitness increased by a mean difference of 2.29 ml/kg/min. Multi-adjusted Cox regression showed a 15% lower risk for the diagnosis of or death from coronary heart disease, or coronary revascularisation per 3.5 ml/kg/min higher peak VO₂ in a healthy and fit population.

Currently, there is no consensus regarding what the prognostic implication is of an increase of 2.29 ml/kg/min in a healthy and fit population. Subgroup analysis reported no difference in peak VO₂, and last 12 weeks. After following the exercise programme, which was primarily based on heart rate at peak VO₂ and lasted 12 weeks. And following it under the supervision of a trained physiotherapist seems to be preferable to no supervision. However, there are complicated and different elements of physical activity and family social support was one of the identified correlated variables. Additionally, the quartiles of some values were transferred to standard deviation, according to Wan et al.21 and Luo et al.6 Subgroup analysis reported no difference in peak VO₂, and the small sample size may be one of the reasons.

Patients after surgery for CHD have significantly lower HRQOL in physical health, and psychosocial health summary scores than healthy controls, according to a cross-sectional survey.26 We assessed it using SF-36, which were public domain questionnaires that included physical and mental components, and CHD-TAAQOL which assessed cardiac-specific aspects of patients with CHD including worries, symptoms, and impact score. No significant differences on the SF-36 and CHD-TAAQOL scales were found between the exercise training and control group. We speculated that this may be due to the small sample size and the fact that most patients had the best-possible scores at baseline. Conversely, Dufier et al.14 reported that participation in an exercise programme improved the HRQOL of post-operative patients with CHD, especially in those with low baseline HRQOL.

Table 1. Exercise training versus controls: VO₂ peak. Review Manager (RevMan) version 5.

| Study or Subgroup | Experimental Mean | SD | Total | Control Mean | SD | Total | Weight | Mean Difference (95% CI) |
|-------------------|-------------------|----|-------|--------------|----|-------|--------|------------------------|
| Avila 2016        | 28.71             | 7.14| 13    | 20.4         | 6  | 19    | 7.0%   | 0.31 [-6.74, 7.36]      |
| Duuppen 2015a     | 38               | 7.64| 24    | 35.2         | 6  | 19    | 15.0%  | 2.00 [-1.91, 7.51]      |
| Duuppen 2015b     | 33.2             | 6.5 | 19    | 32.5         | 6  | 11    | 8.5%   | 0.70 [-5.68, 7.08]      |
| Mosaf 2012        | 33               | 8.2 | 10    | 29.6         | 7.2| 8     | 8.7%   | 3.40 [-2.90, 9.70]      |
| Novakovic 2016a   | 26.88            | 12.51| 9    | 23.5         | 8.0| 4     | 2.0%   | 3.33 [-8.33, 14.99]     |
| Novakovic 2016b   | 24.08            | 6.21| 9    | 23.4         | 8.4| 5     | 4.8%   | 0.54 [-7.83, 8.91]      |
| Therien 2003      | 24.3             | 8.2 | 9     | 22.1         | 6.5| 8     | 7.1%   | 2.20 [-4.60, 9.20]      |
| Vlasek-Bleich 2013| 25.9             | 6.1 | 19    | 23.5         | 5.3| 21    | 27.4%  | 2.40 [-1.16, 5.96]      |
| White 2012        | 28               | 7   | 24    | 26           | 8  | 22    | 18.2%  | 3.00 [-1.36, 7.36]      |
| Total (95% CI)    | 136              |    |       | 102          | 100.0% |       | 2.29 [0.43, 4.15]      |

Heterogeneity: Chi² = 1.01, df = 8 (P = 1.00); I² = 0%
Test for overall effect: Z = 2.41 (P = 0.02)

Conclusion

Our meta-analysis revealed that exercise training should be considered an efficient method of improvement of peak VO₂ in patients after surgery for CHD. Participation in the physical exercise training programme was safe. We recommend that post-operative patients with CHD participate in physical exercise training. To study different forms of exercise training and their effects on quality of life, further research is urgently needed, especially bigger samples and well-designed prospective randomised controlled trials.

Financial support. This work was financially supported by the Science and Technology Fund Project of Tianjin Municipal Health Planning Commission (2014KR16).

Conflicts of interest. None.

Figure 1. Exercise training versus controls: VO₂ peak. Review Manager (RevMan) version 5.
References

1. Moons P, Bovijn L, Budts W, et al. Temporal trends in survival to adulthood among patients born with congenital heart disease from 1970 to 1992 in Belgium. Circulation 2010; 122: 2264–2272.

2. Ávila P, Mercier LA, Dore A, et al. Adult congenital heart disease: a growing epidemic. Can J Cardiol 2014; 30: S410–S419.

3. Amedro P, Dorka R, Moniotte S, et al. Quality of life of children with congenital heart diseases: a multicenter controlled cross-sectional study. Pediatr Cardiol 2015; 36: 1588–1601.

4. Amedro P, Gavotto A, Guillaumont S, et al. Cardiopulmonary fitness in children with congenital heart diseases versus healthy children. Heart 2018; 104: 1026–1036.

5. Voss C, Duncombe SL, Dean PH, de Souza AM, Harris KC. Physical activity and sedentary behavior in children with congenital heart disease. J Am Heart Assoc 2017; 6: 126.

6. Gomes-Neto M, Saquetto MB, da Silva, Silva CM, Conceição CS, Carvalho VO. Impact of exercise training in aerobic capacity and pulmonary function in children and adolescents after congenital heart disease surgery: a systematic review with meta-analysis. Pediatr Cardiol 2016; 37: 217–224.

7. Rychik J, Atz AM, Celermajer DS, et al. Evaluation and management of the child and adult with Fontan circulation: a scientific statement from the American Heart Association. Circulation 2019, CIR0000000000000696.

8. Longmuir PE, Brothers JA, de Ferranti SD, et al. Promotion of physical activity for children and adults with congenital heart disease: a scientific statement from the American Heart Association. Circulation 2013; 127: 2147–2159.

9. Budts W, Pieles GE, Roos-Hesselink JW, et al. Recommendations for participation in competitive sport in adolescent and adult athletes with Congenital Heart Disease (CHD): position statement of the Sports Cardiology & Exercise Section of the European Association for Preventive Cardiology (EAPC), the European Society of Cardiology (ESC) Working Group on Adult Congenital Heart Disease and the Sports Cardiology, Physical Activity and Prevention Working Group of the Association for European Paediatric and Congenital Cardiology (AEPCC). Eur Heart J 2020; 41: 4191–4199.

10. Therrien J, Fredriksen P, Walker M, Granton J, Reid GJ, Webb G. A pilot study of exercise training in adult patients with repaired tetralogy of Fallot. Can J Cardiol 2003; 19: 685–689.

11. Moalla W, Elloumi M, Chamari K, et al. Training effects on peripheral muscle oxygenation and performance in children with congenital heart diseases. Appl Physiol Nutr Metab 2012; 37: 621.

12. Winter MM, van der Bom T, de Vries LC, et al. Exercise training improves exercise capacity in adult patients with a systemic right ventricle: a randomized clinical trial. Eur Heart J 2012; 33: 1378–1385.

13. Westhoff-Bleck M, Schieffer B, Tegtbjer U, et al. Aerobic training in adults after atrial switch procedure for transposition of the great arteries improves exercise capacity without impairing systemic right ventricular function. Int J Cardiol 2013; 170: 24–29.

14. Duller K, Duppen N, Kuipers IM, et al. Aerobic exercise influences quality of life of children and youngsters with congenital heart disease: a randomized controlled trial. J Adolesc Health 2014; 55: 65–72.

15. Duppen N, Ettel JR, Spaans L, et al. Does exercise training improve cardiopulmonary fitness and daily physical activity in children and young adults with corrected tetralogy of Fallot or Fontan circulation? A randomized controlled trial. Am Heart J 2015; 170: 606–614.

16. Ávila P, Marcotte F, Dore A, et al. The impact of exercise on ventricular arrhythmias in adults with tetralogy of Fallot. Int J Cardiol 2016; 219: 218–224.

17. Novaković M, Prokšelj K, Rajkoš u, et al. Exercise training in adults with repaired tetralogy of Fallot: a randomized controlled pilot study of continuous versus interval training. Int J Cardiol 2018; 255: 37–44.

18. Williams CA, Wadey C, Pieles G, Stuart G, Taylor RS, Long L. Physical activity interventions for people with congenital heart disease. Cochrane Database Syst Rev 2020; 10: CD013400.

19. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev 2015; 4: 1.

20. Higgins JP, Altman DG, Gotzsche PC, et al. The Cochrane Collaboration’s tool for assessing risk of bias in randomised trials. BMJ 2011; 343: d5928–d5928.

21. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. BMC Med Res Methodol 2014; 14: 135.

22. Luo D, Wu X, Liu J, Tong T. Optimally estimating the sample mean from the sample size, median, mid-range, and/or mid-quartile range. Stat Methods Med Res 2018; 27: 1785–1805.

23. Moalla W, Elloumi M, Chamari K, et al. Training effects on peripheral muscle oxygenation and performance in children with congenital heart diseases. Appl Physiol Nutr Metab 2012; 37: 621–630. DOI 10.1139/h2012-036.

24. Udhom S, Aldrie KB, Hjordtke VE, Veldtman GR. Prognostic power of cardiopulmonary exercise testing in Fontan patients: a systematic review. Open Heart 2018; 5: e000812.

25. Letnes JM, Dalen H, Vesterbekkmo EK, Wisloff U, Næs BM. Peak oxygen uptake and incident coronary heart disease in a healthy population: the HUNT Fitness Study. Eur Heart J 2019; 40: 1633–1639.

26. Mellion K, Uzark K, Cassidy A, et al. Health-related quality of life outcomes in children and adolescents with congenital heart disease. J Pediatr 2014; 164: 781–788.e1.

27. Bauman AE, Reis RS, Sallis JF, et al. Correlates of physical activity: why are some people physically active and others not? Lancet 2012; 380: 258–271. DOI 10.1016/S0140-6736(12)60735-1.

28. Sutherland N, Jones B, Westcamp Aguero S, et al. Home- and hospital-based exercise training programme after Fontan surgery. Cardiol Young 2018; 28: 1299–1305. DOI 10.1017/S1047951118001166.