Review Article

Paediatric cardiac rehabilitation in congenital heart disease: a systematic review

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Abstract Background: Advances in medical and surgical care have contributed to an important increase in the survival rates of children with congenital heart disease. However, survivors often have decreased exercise capacity and health-related issues that affect their quality of life. Cardiac Rehabilitation Programmes have been extensively studied in adults with acquired heart disease. In contrast, studies of children with congenital heart disease have been few and of limited scope. We therefore undertook a systematic review of the literature on cardiac rehabilitation in children with congenital heart disease to systematically assess the current evidence regarding the use, efficacy, benefits, and risks associated with this therapy and to identify the components of a successful programme. Methods: We included studies that incorporated a cardiac rehabilitation programme with an exercise training component published between January, 1981 and November, 2010 in patients under 18 years of age. Results: A total of 16 clinical studies were found and were the focus of this review. Heterogeneous methodology and variable quality was observed. Aerobic and resistance training was the core component of most studies. Diverse variables were used to quantify outcomes. No adverse events were reported. Conclusions: Cardiac Rehabilitation Programmes in the paediatric population are greatly underutilised, and clinical research on this promising form of therapy has been limited. Questions remain regarding the optimal structure and efficacy of the programmes. The complex needs of this unique population also mandate that additional outcome measures, beyond serial cardiopulmonary exercise testing, be identified and studied.

Keywords: Exercise; quality of life; children

Received: 7 August 2011; Accepted: 17 November 2011; First published online: 17 January 2012

THE INCIDENCE OF CONGENITAL HEART DISEASE IS 4 to 8 per 1000 live births.¹ Although advances in medical knowledge and technology have, over the past few decades, dramatically improved the survival of children with congenital heart defects, for many lesions life expectancy of patients remains short and quality of life low.²⁻⁴ Residual cardiovascular defects are responsible for some of these hardships. Survivors of congenital heart disease are also often afflicted with pulmonary, neurological, neurodevelopmental, orthopaedic, and other comorbidities that impair their ability to function.^{5–8} Superimposed upon these physical impairments, patients with congenital heart disease are often subject to overprotection on the part of parents, educators, and healthcare providers predisposing them to physical inactivity and exercise intolerance.^{9,10}

These factors can have serious implications for congenital heart disease survivors' long-term health and quality of life. In adults, physical inactivity has been found to be an independent risk factor for atherosclerosis, cardiovascular disease, and diabetes.¹¹ Indeed, sedentary living is estimated to be responsible

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for approximately one-third of deaths due to coronary heart disease and type II diabetes, and low cardiopulmonary fitness is a strong independent predictor of all-cause mortality. Among adults, the relative risk for cardiovascular death that is associated with being unfit exceeds that associated with smoking, elevated systolic blood pressure, hypercholesterolaemia, or obesity.^{11–13} Among patients with congenital heart disease, diminished exercise capacity has been found to be an independent predictor of death/and or hospitalisation for individuals with repaired Tetralogy of Fallot, Transposition of the Great Arteries, Pulmonary Hypertension, and Fontan Physiology.^{13–17} To optimally manage patients with complex congenital heart disease, the role of ancillary therapies that may not cure but may potentially improve cardiac function and quality of life – such as cardiac rehabilitation - should be explored.¹²

Cardiac rehabilitation programmes have been widely studied in adults with acquired heart disease. Programmes for acute - post-MI or post-surgery and chronic patients differ with regard to the intensity of endurance training, the level of monitoring employed, and the number/training of the personnel required for supervision; other aspects of the programmes are similar. In addition to improving oxygen consumption and exercise capacity, they have been found to reduce morbidity, mortality, and economic costs, as well as improve quality of life.¹⁸⁻²¹ They also have a salutary effect upon standard cardiovascular risk factors such as lipid profiles, adiposity, and hypertension. The effects of exercise on these conventional cardiovascular risk factors are, however, substantially less compared with those achieved by pharmacological therapies alone, and the mortality benefits associated with exercise and fitness cannot be explained solely by the impact of these dynamics upon the conventional risk factors.^{11,22–24}

Unfortunately, only 10% of all potential adult candidates for exercise training/cardiac rehabilitation actually receive this therapy. Among children this percentage is much lower.

One would expect that the benefits associated with exercise training in adults with cardiovascular disease would also be recognised among children with congenital heart disease. However, there have been relatively few clinical studies of paediatric cardiac rehabilitation. These studies vary greatly in design, inclusion criteria, assessment of risk factors, duration of follow-up, attrition, and particularly in outcome measures. Thus, a systematic review of the existing literature is needed to summarise and evaluate the existing data regarding the benefits of cardiac rehabilitation in children, to determine the proper outcome measurements, and to identify the attributes of a successful programme.

Methods

Search strategy: The bibliographical search was performed using the following strategy: heart, cardiac, rehabilitation, exercise, lung, human, infant, child, adolescent.

The databases searched during the study were: MEDLINE/PubMed, EMBASE, Cardiosource Clinical Trials Database, and Cochrane Library. Additional studies were obtained from the bibliography of the studies obtained.

Inclusion criteria: Studies were included if they contained a structured cardiac rehabilitation programme with an exercise training component in cardiac patients up to 18 years of age or if they reviewed these types of studies. Only complete articles published from January, 1981 until November, 2010 were included.

Exclusion criteria: Languages other than English, Spanish, French, or Italian or studies with a rehabilitation component but without an exercise training component were not included.

Classification of the evidence: Two independent authors reviewed each paper. Each reviewer classified each study according to the OXFORD classification for evidence-based medicine²⁵ – a classification system based on the type of study (Table 3). When the authors' classifications differed, the case was discussed and a consensus classification was determined. The quality of the evidence supporting the use of cardiac rehabilitation in children with congenital heart disease was then graded, based upon the entirety of the studies reviewed, as described by the Oxford Center for Evidence-Based Medicine (Table 4).

Results

A total of 193 articles were found; however, only 24 met our inclusion criteria. Of these, 21 had a structured rehabilitation programme, but only 18 had an exercise training component. These papers are the focus of this review. Of these articles, two were case reports and were not included in our final analysis.^{12,26} The youngest patients included were 4 years old. The number of patients included per study ranged from 1 to 103, and the duration of the programme ranged from 2 weeks to 10 months. No adverse events were reported. The essential features of each study are summarised in Tables 1 and 2.

The level of evidence of these studies was scored according to the OXFORD classification system and is presented in Table 3. There were no randomised control trials, and the best studies receive a score of only 3. Overall, the level of evidence supporting the efficacy of cardiac rehabilitation in children with

References	Location	Patient population	Ages	n	Patients treated	Type of excercise	Duration	Frequency	Intensity	Sessions
McBride ⁴²	Hospital	Heterogeneous	10–16	20	20	Aerobic, resistance	2–10 months	3/week	HR at AT, 60% of maximal voluntary contraction	30–60 min
Rhodes ³⁰	Hospital	Heterogeneous	8-18	33	15	Aerobic, resistance	3 months	2/week	HR at AT, light resistance	60 min
Moalla ²⁸	Home	Heterogeneous	12-15	18	10	Aerobic	12 weeks	3/week	HR at AT	45 min
Brassard ³⁹	Home (2), hospital (3)	Fontan	11–26	5	5	Aerobic, resistance	2 months	3/week	50–80% peak VO ₂	20-30 min
Opocher ³¹	Hospital + home	Fontan	7-12	10	10	Aerobic	8 months	2/week	50–70% peak VO ₂	30–45 min
Rhodes ²⁷	Hospital	Heterogeneous	8-17	16	16	Aerobic, resistance	3 months	2/week	HR at AT, light resistance	60 min
Minamisawa ²⁹	Home	Fontan	11-25	11	11	Aerobic	2-3 months	2-3/week	60–80% peak HR	40 min
Fredriksen ³²	Hospital or supervised gym	Heterogeneous	10–16	93	55	Aerobic, resistance, flexibility, education	2 weeks or 5 months	Daily or 2/week	65–80% peak HR	Not specified
Sklansky ³³	Hospital	TOF	6–16	11	11	Aerobic	2 months	3/week	60–70% peak HR	30 min
Balfour ³⁴	Hospital	Heterogeneous	13.5–19.8	6	6	Aerobic, education	3 months	3/week	>70% peak HR	30–40 min
Calzolari ³⁸	Hospital	TOF	6–16.5	18	9	Aerobic, respiratory	3 months	3/week	60–70% peak HR	60 min
Longmuir ⁴³	Home	Heterogeneous	4.7–14.3	40	17	Aerobic, resistance, flexibility, coordination	6 weeks	2/week	Capability of talking during exercise	Not specified
Longmuir ⁴⁴	Home	Heterogeneous	4.7–14.3	60	30	Aerobic, resistance, flexibility, coordination	6 weeks	2/week	Capability of talking during exercise	Not specified
Bradley ⁴⁵	Hospital	TOF/TGA	4–13	9	9	Aerobic, resistance, flexibility, coordination	12 weeks	2/week	60–80% peak HR	60 min
Ruttenberg ⁴⁰	Hospital	Heterogeneous	7-18	21	21	Aerobic	9 weeks	3/week	65–75% peak HR	30 min
Goldberg 41	Home	TOF/VSD	7-18	26	26	Aerobic	6 weeks	3–4/week	50–70% peak VO_2	45 min

Table 1. Description of patient population and rehabilitation programme.

https://doi.org/10.1017/S1047951111002010 Published online by Cambridge University Press

AT = anaerobic threshold; HR = heart rate; TGA = transposition of the great arteries; TOF = tetralogy of Fallot; VSD = ventricular septal defect; VO₂ = oxygen consumption

References	Type of study	Follow-up period	Outcome variables	Results	Comments
McBride ⁴²	Case series	Immediately post programme	Safety	No major complications.	No CPX data
Rhodes ³⁰	NRCT [*]	5 years post programme	 Serial cardiopulmonary exercise testing Activity, self-esteem and emotional state questionnaires 	 Significant increase (p < 0.01) in: peak work rate (7.8%) peak VO₂ (21.8%) Non-significant decline in these parameters in control group 	 Well-controlled study RER reported Examined midterm effects of the intervention and quality of life
Moalla ²⁸	NRCT [*]	Immediately post programme	 Serial cardiopulmonary exercise testing Respiratory muscle oxygenation (near- infrared spectroscopy) 	 Significant increase in: peak VO₂ (21%; p < 0.05) peak respiratory muscle oxygenation (22%; p < 0.01) Significant correlation between tissue oxygenation and peak VO₂ at AT (p < 0.01) Non-significant improvement in pulmonary function was observed in the training group 	 Home exercised regime Compliance not assessed RER not reported Suggests that respiratory physiotherapy in the programme might be helpful
Brassard ³⁹	Case series	Immediately post programme	 Serial cardiopulmonary exercise testing Muscle strength (Dynamometer) Blood pressure Ergoreflex 	 Non-significant increase in: peak VO₂ (p = 0.47) muscle strength (p = 0.57) Significative ergoreflex contribution to systolic blood pressure (p = 0.02) 	 Short duration and variable programme structure might account for lack of improvement
Opocher ³¹	Case series	Immediately post programme	• Serial cardiopulmonary exercise testing	 Significant increase in: estimated workload (11.3%; p = 0.03) O₂ pulse (19%; p = 0.004) Non-significant increase: 	• RER not reported

• peak VO₂ (11%; p = 0.07)

https://doi.org/10.1017/S1047951111002010 Published online by Cambridge University Press

References	Type of study	Follow-up period	Outcome variables	Results	Comments
Rhodes ²⁷	Case series	Immediately post programme	• Serial cardiopulmonary exercise testing	 Significant increase (p < 0.01) in: peak work rate (14%; p < 0.001) peak VO₂ (16.3%; p 0.005) %predicted? predicted O₂ pulse (27.6%; p = 0.01) FEV1 (7%; p < 0.001) 	No control groupRER reported
Minamisawa ²⁹	Case series	Immediately post programme	• Serial cardiopulmonary exercise testing	 Significant increase in: 7% workload (p = 0.04) 7% peak VO₂ (p = 0.03) Significant decrease in: HR with sub-maximal effort (p < 0.05) 	 Home programmes might be a more economical option but compliance is more difficult to assess RER not reported
Fredriksen ³²	NRCT [*]	Immediately post programme	 Serial cardiopulmonary exercise testing Activity monitor (accelerometer) Psychosocial function (youth self-report and child behaviour checklist) 	 Significant increase in: peak VO₂ (1.67 ± 0.57 versus 1.82 ± 0.661 × min⁻¹; p < 0.001) exercise time (614 ± 138 versus 655 ± 155 s; p = 0.005) activity (p 0.028) and psychosocial (p < 0.001) levels 	 Large study population Varied activities might have enhanced patient compliance One of the few to incorporate education RER reported
Sklansky ³³	Case series	Immediately post programme	 Serial cardiopulmonary exercise testing Ventricular function (echocardiography) 	 Significant increase in: endurance time (1.7 min; p < 0.0004) Significant decrease in: sub-maximal heart rate (p < 0.001) No increase in: ectopy with exercise arrhythmias 	Retrospective studyRER not reported

Table 2. Continued

References	Type of study	Follow-up period	Outcome variables	Results	Comments
Balfour ³⁴	Case series	Immediately post programme	• Serial cardiopulmonary exercise testing	 Significant increase in: peak VO₂ (20%; p < 0.005) endurance time (21%; p < 0.03) Significant decrease in: systolic blood pressure (7%; p < 0.03) 	 Includes stress management and nutrition counselling RER not reported High drop-out rate
Calzolari ³⁸	NRCT [*]	Immediately post programme	• Serial cardiopulmonary exercise testing	Non-significant increase in: • maximal • sub-maximal exercise capacity	No CPX dataRespiratory therapy included
Longmuir ^{43,44}	NRCT [*]	5 years post programme and immediately post programme	• Exercise test (Canada fitness awards test: cardiovascular endurance, strength, flexibility, and coordination)	 Significant increase (p < 0.01) in: different scores at 6 months and 5 years post programme 	 Large patient population Control group No CPX testing Long-term follow-up
Bradley ⁴⁵	Case series	Immediately post programme	 Anthropometric measurements Serial cardiopulmonary exercise testing 	 Significant increase in: peak systolic pressure (17%; p < 0.001) peak VO₂ (20%; p < 0.01) endurance time (18%; p < 0.01) 	 Youngest study population One of the most complete programmes RER not reported
Ruttenberg ⁴⁰	NRCT [*]	Immediately post programme	• Basic exercise test	 Significant increase: endurance time (p < .01) non-significant increase in peak VO₂ (p = 0.1) 	RER not reportedSub-optimal control group
Goldberg ⁴¹	Case series	Immediately post programme	 Exercise capacity (cyclergometer) Body composition 	 Significant increase: maximal work capacity (p < 0.001) Non-significant increase: peak VO₂ peak HR Improvement of body composition 	• Short programme duration

AT = anaerobic threshold; CPX = cardiopulmonary testing; FEV1 = forced expiratory volume in the first second; HR = heart rate; NRCT = non-randomized controlled tria; RER = respiratory exchange ratio; VO_2 = oxygen consumption

*NRCT – equivalent to a cohort study in the modified CONSORT definition⁵⁶

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Table 3. Levels of evidence.

References	Level of evidence
McBride ⁴³	4
Rhodes ³⁰	2B
Moalla ²⁸	2B
Brassard ³⁹	2B
Opocher ³¹	4
Rhodes ²⁷	3B
Minamisawa ²⁹	4
Fredriksen ³²	2B
Sklansky ³³	4
Balfour ³⁴	4
Calzolari ³⁸	2B
Longmuir ⁴³	2B
Longmuir ⁴⁴	2B
Bradlev	4
Ruttenberg ⁴⁰ Goldberg ⁴¹	2B
Goldberg ⁴¹	4

Table 4. Classification of level of evidence.

Level of evidence	Type of study
1	Systematic review of randomized trials
2	Individual randomized control trial or observational study with dramatic effect
3	Non-randomized controlled cohort/follow-up study
4	Case series, case-control studies or historically controlled studies
5	Mechanism-based reasoning

congenital heart disease may be characterised as suggestive but not as definitive (Oxford Center for Evidence-Based Medicine Classification B; Table 4).

Discussion

The main goal of this review was to describe and quantify existing data regarding rehabilitation programmes for children with congenital heart disease. Several studies have found evidence supporting the acute benefits of cardiac rehabilitation in these patients.^{27–35} Serious adverse events have not been encountered. A limited number of previous reviews have evaluated this subject^{36,37} and have, in general, concurred with these findings.

However, our review raises a number of important issues that have not been previously addressed. Beneficial results were not uniformly observed and adequate randomisation was not often employed. It must also be acknowledged that the physiologic alterations and residual impairments associated with different congenital heart defects vary greatly, and the response to rehabilitation may differ depending upon the defects present. Ideally, each pathologic variant should be studied individually. However, only seven of the clinical trials studied a homogenous population.^{12,26,29,31,33,38,39}

The structure of the rehabilitation programmes also varied considerably with regard to the intensity, frequency, and duration of exercise. Most early studies also limited their training programmes to aerobic exercises.^{27,29,31,33,34,38,40,41} In contrast, most current rehabilitation programmes employ a combination of aerobic and resistance training.^{12,26,28,32,39,42–45} Owing to the fact that a strong relationship exists between muscle strength and exercise tolerance,^{12,36} suboptimal training regimen may account for the ambiguous results that emerged from some of the paediatric rehabilitation programmes.

However, even the current rehabilitation programmes do not take into account the fact that congenital heart disease may also be associated with congenital or acquired abnormalities in other organ systems, which may be appropriately addressed in rehabilitation therapy. These organ systems include:

Pulmonary: Coexisting pulmonary pathology is common among patients with congenital heart disease including restrictive lung disease, obstructive lung disease, diaphragmatic paralysis, recurrent pulmonary infections, etc. Although pulmonary dysfunction is usually not the main factor limiting exercise capacity,⁴⁶ it could contribute to exercise limitation during a maintained submaximal effort. Respiratory physiotherapy may therefore improve the congenital heart disease patient's cardiorespiratory response to exercise, just as it does in patients with chronic heart failure.^{5,28,46–48}

Neurologic: The neurologic deficits encountered among patients with congenital heart disease may range from major syndromes such as hemiparesis, cerebral palsy, or epilepsy to more subtle symptoms such as neurodevelopmental delays, learning disabilities, or attention deficit disorders.^{6–8} These disabilities may be appropriate targets for rehabilitation therapy and/or may influence the structure of an individual's rehabilitation programme.

Musculoskeletal: Musculoskeletal abnormalities are among the most common extracardiac anomalies associated with congenital heart disease. These patients may have scoliosis and other thoracic deformities, connective tissue disorders, hypotonia, etc.^{49,50} all of which may be relevant to one or more aspects of a patient's rehabilitation programme.

Few of the paediatric cardiac rehabilitation programmes reviewed here incorporated features designed to address these issues and most did not include recommended components of adult rehabilitation programmes,²⁰ such as nutritional counselling, aggressive risk factor management,

psychosocial and vocational counselling, physical activity counselling, education, and psychological intervention. Indeed, educational intervention, one of the main pillars in adult cardiac rehabilitation, was employed in only four of the trials.^{12,32,34,45} Similarly, psychological assessment/counselling was never included. Owing to the fact that behavioural issues are not uncommon among children with congenital heart disease and their caretakers^{6–8}, these omissions may have significant negative consequences and decrease the success rate of a cardiac rehabilitation intervention.

Mid/long-term follow-up data have been provided by only two studies (Longmuir⁴³ and Rhodes³⁰). Significant improvements, persisting beyond the immediate post-programme period, were observed. These studies suggest that rehabilitation programmes can have persistent beneficial effects in children with congenital heart disease. However, it is difficult to draw firm conclusions from these two, small studies. Certainly, to reliably achieve longstanding lifestyle changes - a necessity for these patients with a chronic disease, and one of the major goals of cardiac rehabilitation - a multi-level intervention that targets the children, their lifestyles, and their caretakers seems desirable. To sustain acute improvements, reinforcement with long-term followup programmes should be pursued. These approaches have been productively incorporated into exercise programmes for children with obesity.51,52 The outcomes of obesity programmes that incorporate these multidimensional features have been found to be superior to those of programmes with more limited resources.⁵¹ Better results may also accrue to children with congenital heart disease if their rehabilitation programmes were to be enhanced with these capabilities.

The technology used to assess the impact of cardiac rehabilitation also varied considerably from study to study. Serial cardiopulmonary exercise testing – one of the most valuable tools for objectively and quantitatively assessing the impact of cardiac rehabilitation – was used in a fraction of the studies. The respiratory exchange ratio – probably the best objective measure of effort expenditure in this population – often was not reported or used to establish that the observed changes were due to the effects of the rehabilitation programme rather than the variations in effort expenditure. It is therefore difficult to reliably interpret the peak exercise data of these studies.

Apart from the peak oxygen consumption, there is no consensus regarding the other outcome measures that should be used to assess the effects of cardiac rehabilitation. Potential candidates include muscle strength,¹² body composition, quality of life questionnaires, etc. In order to fully assess the effects and benefits of a cardiac rehabilitation programme, variables that reliably measure the impact of the programme upon the different areas affected by congenital heart disease must be identified and studied.

From the articles reviewed for this study, and the literature regarding exercise programmes for patients with obesity and other chronic paediatric diseases, such as cystic fibrosis⁵³ and renal transplantation,^{54,5} there appears to be a consensus that rehabilitation programmes should have a duration of at least 12 weeks and a frequency of two to three times a week, with sessions lasting at least 40 minutes. We believe that the programmes should include aerobic, resistance, and flexibility training, as well as education and psychological intervention. The intensity of aerobic exercise should be at a heart rate approximately equivalent to that associated with the anaerobic threshold. This consideration is particularly relevant to children with congenital heart disease, as chronotropic impairment is commonly encountered in this population.

A final point that emerges from this analysis is that rehabilitation programmes for children with congenital heart disease are underutilised and their potential value underappreciated. A number of factors may account for this state of affairs, including systematic deficiencies, for example, a limited number of specialised facilities/personnel; economic limitations, for example, a lack of insurance coverage for the programmes; provider unawareness, for example, healthcare providers underestimate the value and/or availability of rehabilitation programmes; and patient-related factors, for example, logistic problems, expense, parental anxiety. Resolution of these issues will require changes at various levels of healthcare policies, protocols and increasing awareness of these programmes among healthcare dispensers and families.

Conclusion

We are now confronted with a growing patient population of survivors of congenital heart disease. These individuals continue to suffer from disabilities that affect their present and future quality of life. Multidisciplinary interventions, such as cardiac rehabilitation, which could greatly benefit many of these patients, are underappreciated and almost invariably overlooked as a first-line approach to secondary intervention.

Benefits have been observed in many studies of cardiac rehabilitation in children with congenital heart disease, and no adverse events have been reported. Although challenging at various levels, randomised controlled studies on larger homogeneous population are needed to prove the efficacy of these interventions, stratify risk in these patients, and develop optimal protocols. Long-term effects and outcomes should be determined.

The chosen outcome variables have also been incomplete. Ideally, they should assess the effects of the programme on multiple areas including impairment of body structures or functions, limitation of activities, and restriction of participation. Serial cardiopulmonary exercise testing is best suited for measuring exercise capacity and prescribing exercise intensity. Other modalities should be developed to quantitatively assess other areas of impairment.

The optimal structure of a paediatric cardiac rehabilitation programme also remains unclear. A combination of aerobic and resistance exercise is probably ideal. Including complementary therapies such as respiratory physiotherapy, education and psychological interventions might improve the outcome of these programmes; however, this issue has not been thoroughly studied. Comorbidities and environmental impediments that often confront patients with congenital heart disease have, historically, not been addressed by rehabilitation programmes. The role of parents in the rehabilitation programmes has also been overlooked. These are areas that deserve greater attention. We believe that a cardiac rehabilitation programme should be based on multidisciplinary interventions that apply a holistic approach to the patient and treat the ensemble of problems that they confront.

Acknowledgement

Grant: Research Fellowship Grant Fundación Alfonso Martin Escudero for Dr Ana Ubeda

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