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Review

Systematic review of the effects of physical exercise training programmes in children and young adults with congenital heart disease ☆

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ABSTRACT

Background: Most patients with congenital heart disease (ConHD) do not perform regular physical exercise. Consensus reports have stated that exercise should be encouraged and regularly performed in these patients, but this is not common practise. We reviewed the literature on actual evidence for either negative or positive effects of physical exercise training programmes in children and young adults with ConHD.
Methods: Using the Medline database, we systematically searched for articles on physical exercise training programmes in ConHD.
Results: A total of 31 articles met all inclusion criteria; in total, 621 subjects (age range 4 to 45 years) were included. Most studies used training programmes with a duration of 12 weeks. On average, the number of training sessions was 3 times per week. In 12 studies, training intensity was set at a percentage of peak heart rate.
Outcome measures reported were PeakVO_2, activity levels and muscle strength. Twenty-three studies (72%) found a significant positive change in the main outcome measure after the physical exercise training period. None of the studies reported negative findings related to physical exercise training in ConHD. Cardiac effects have hardly been studied.
Conclusion: In most studies, participation in a physical exercise training programme was safe and improved fitness in children and young adults with ConHD. We recommend that patients with ConHD participate in physical exercise training. Cardiac effects need to be studied more extensively.

1. Introduction

Most patients with congenital heart disease (ConHD) are less active than healthy peers and do not participate in regular exercise programmes [1]. This limited physical activity may be the result of residual haemodynamic problems, chronotropic impairment as well as psychosocial factors such as parental overprotection or restraints imposed by patients' social surroundings [2,3]. Studies in the field of acquired heart diseases have shown that reduced levels of daily activity are strong predictors of poor outcome, including early death [4]. Physical exercise training programmes in patients with acquired cardiovascular disease have resulted in a reduction in mortality and morbidity [5]. Patients with ConHD who participate in sports from an early age have a significantly lower chance of becoming sedentary adults [6,7].

European consensus reports in 2006 and 2011 stated that exercise should be performed and encouraged in ConHD patients [8,9]. Nevertheless, many practitioners are reluctant to recommend exercise for ConHD patients since knowledge of cardiac effects and risks related to exercise is scarce [10].

Furthermore, outcome parameters and predictors for success of exercise programmes have not been firmly established. Increased maximal oxygen uptake derived from cardiopulmonary exercise testing (CPET) is commonly used. While this parameter has been shown to be an excellent surrogate marker for long-term outcome in patients with ConHD [11], other factors such as changes in activity level and muscle strength are factors to consider in evaluating the effect of the training programme [12].

The aim of the current review was to assess the negative or positive effects of physical exercise training programmes in children and young adults with ConHD.

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Table 1
Study design.

Reference	Year of publication	Age years range/mean ± SD	Training group N	Control group N	Drop out pt/controls (% of all participants)	Overall training not participated %	Duration week	Training/week N (voluntarily)	Time per session minutes	Training intensity	Training implementation
Müller [26]	2012	4–6	14	0	–	–	12	1	60	–	Supervised
Cordina [20]	2012	21–41[$]	9	7‡	3/2 (31%)	24 ± 5%	20	3	60	–	Supervised
Moalla [27]	2012	12–15	10	8‡	0	–	12	3	60	HR at Vth	Home (HR monitor)
Winter [17]	2011	32 ± 11	28	26‡	4/4 (15%)	–	10	3	42	Incremental 60% to 90% PeakHR	Home (HR monitor; weekly email contact)
Martinez-Quintana [21]	2010	18–38	4	4‡	0	–	12	2	34 + resistance training	80% PeakHR	Supervised
Dua [28]	2010	32 ± 11	61	0	11 (18%)	–	10	5	5 to 30 min + 10% each week	Based on METS	Home (twice weekly telephone contact)
Amaird [22]	2008	15 ± 1	13	10‡	–	–	8	3	60	DT-level	Home (HR monitor, checked every week)
Lichtman [43]	2008	28	1	0	0	0	–	–	–	RPE driven	Supervised
Singh [29]	2007	12 ± 2	14	15‡	–	–	12	2 (2)	60	–	Home and/or supervised
McBride [30]	2007	14 ± 3	20	0	0	17%	Until HTx (6 ± 4 months)	3	60	HR at Vth and 60% perceived voluntary contraction	Supervised
Rhodes [15,16]	2005–06	8–16	19	0	3 (16%)	25%	12	2 (2)	60	HR at Vth	Home and/or supervised
Moalla and Maingourd [23]	2006	12–15	10	8‡	0	–	12	3	60	HR at Vth	Home (HR monitor)
Brassard [31]	2006	11–26	5	4‡	–	–	8	3	20–30	HR at 50–80% PeakVO$_2$ + resistance training	Home or supervised
Moalla and Gautier [18]	2005	12–16	9	8‡	0	–	12	3	60	HR at Vth-level	Home (HR monitor, checked every week)
Opocher [32]	2005	6–12	10	0	0	9 pt < 10%; 1 pt > 90%	32	2	30–45	50–70% PeakVO$_2$	Home and supervised (HR monitor, monthly telephone contact)
Therrien [19]	2003	25–45[$]	9	9‡	0/1 (6%)	20%	12	3	30–50	60–85% PeakVO$_2$	Home and supervised (diary)
Minamisawa [33]	2001	19 ± 4	16	0	5 (31%)	–	8–12	2–3	25–36	HR at 60–80% PeakHR	Home and/or supervised (telephone contact)
Fredriksen [24]	2000	10–16	55	38‡	36 (39%)*	–	2 or 20**	–/2***	–	65–80% PeakHR	Supervised (centre or near home) (HR monitor)
Sklansky [34]	1994	6–16	13	0	2 (15%)	–	8	3	30	60–70% PeakHR	Supervised
Balfour [35]	1991	17 ± 3	16	0	9 (56%)	19%	12	3 (2)	30–40	70% PeakHR	Home and supervised
Calzolari [37]	1990	6–17	9	9‡	0	10%	12	3	60	60–70% PeakHR	Supervised
Tomassoni [36]	1990	5–15	12	0	4 (33%)	–	12	2–3	30–60	60–80% PeakHR	Home and supervised
Longmuir [13,14]	1985–90	5–14	29	31‡	2 (3%)	–	At least 6	2 (5)	–	–	Home and supervised (biweekly telephone contact)
Peja [25]	1990	8 ± 4	20	20‡	–	–	52	2–3 (–)	45/–	HR 120–150 b/min	Home and supervised
Vaccaro [38]	1987	5–12	5	0	–	–	12	2–3	30–60	60–80% PeakHR	Home and supervised
Bradley [39]	1985	4–13	11	0	2 (18%)	–	12	2–3	25–60	60–80% PeakHR	Home and supervised
Ruttenberg [40]	1983	7–18	24	26†	12/17 (58%)	–	9	3	5–30	65–75% PeakHR	Supervised
Mathews [41]	1983	12–20	7	7†	3/3 (43%)	18%	52	3	50	75–80% PeakHR	Supervised
Goldberg [42]	1981	14 ± 3	26	0	0	31%	6	3–4	45	50–70% PeakWL	Home (diary and weekly telephone contact)

HR: heart rate; Vth: ventilatory threshold; METS: metabolic equivalent taks; DT: dyspnea threshold; RPE: rating perceived exertion; HTx: heart transplantation; PeakVO^2: ventilatory oxygen peak; b/min: beats per minute and PeakWL: workload peak.

‡ Control group consists of subjects with a ConHD who do not train.

† Control group consists of healthy subjects who do train.

* 38 patients were excluded after enrolment, it is not mentioned in which group they participated.

** 2 weeks training in rehabilitation centre or 20 weeks training in a home based centre.

*** Training per week not mentioned in rehabilitation centre based study.

$ Article defines age per category: Cordina: training group 31 ± 10, control group 33 ± 2; and Therrien: training group 35 ± 10, control group 33 ± 7.

Rehabilitation programme starts in hospital after surgery; period is not defined; after discharge the programme continues for 6 weeks at home.

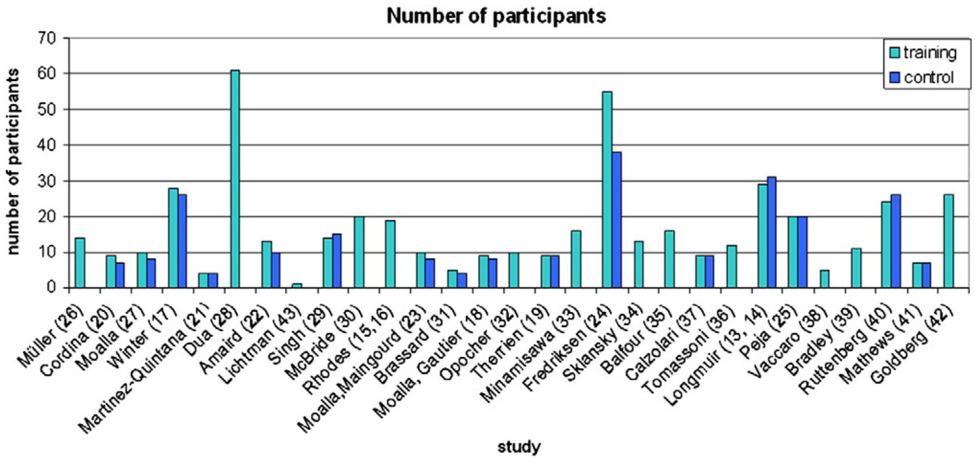

Fig. 1. Number of participants per study, if applicable; summarised per group. Ordered by year of publication, the oldest publication is placed last.

2. Methods

The Medline database was used to search for articles published between 1960 and December 2012 regarding physical exercise in congenital heart disease. The first search term used was: training OR cardiac rehabilitation OR aerobic training OR exercise performance OR exercise training OR rehabilitation OR physical exercise OR physical training OR exercise rehabilitation OR exercise programme OR aerobic exercise training OR exercise. The second search term, which could be either in the title or the abstract, was: congenital heart disease, OR congenital heart diseases. The search was performed by one of the authors (ND).

The abstracts of relevant articles were screened on the basis of the following criteria: the study population or part of the study population had to have a diagnosed congenital heart disease and intervention had to consist of any type of exercise. If the data in the abstract met the inclusion criteria, the full-text paper was studied. Further reference lists of articles were checked to retrieve articles that met the inclusion criteria but were not registered in Medline.

The following data were extracted: study design, the nature of ConHD, the nature of any surgery performed; participants' gender, age and age range; the size of the study population and of any control group; the number of drop outs; the type of exercise; the number of training sessions, their duration and locations (home or supervised at an allocated centre); and percentage of training sessions which were not performed. The result sections were studied and all results relevant to the training intervention were extracted and interpreted. Results were categorised in adverse events, short-term effects on the heart, on exercise capacity, on muscle strength and activity levels, and on long-term effects on exercise capacity.

3. Results

The initial search strategy on exercise training produced 191 articles. A total of 31 articles met all inclusion criteria. In these 31 articles 29 study populations were described, of 2 of these populations the short-term and long-term effects were reported in separate articles

Table 2
Distribution of types of congenital heart disease in the populations in the studies included.

Reference	ToF (n)	Fontan (n)	TGA (n)	Left obstructive lesions (n)	Right obstructive lesions (n)	L–R shunts (n)	Other (n)	TOTAL
Müller [26]	2	1	1	4	3	3		14
Cordina [20]		11						11
Moalla [27]	5	4	5			4		18
Winter [17]		54						54
Martinez-Quintana [21]		4*	2*			1*		7
Dua [28]	8	4	5	10	3	7	13	50
Amiard [22]	5		5			5	8	23
Lichtman [43]		1						1
Singh [29]		11					3	14
Mcbride [30]		4					16	20
Rhodes [15,16]		11	1		2	1	1	16
Moalla and Maingourd [23]	5	4	5			4		18
Brassard [31]		7						7
Moalla and Gautier [18]	4	4	7			2		17
Opocher [32]		10						10
Therrien [19]	17							17
Minamisawa [33]		16						16
Fredriksen [24]	16	17	6	20	9	16	9	93
Sklansky [34]	11							11
Balfour [35]	1	2		3	1	2	7	16
Calzolari [37]	9							9
Tomassoni [36]	2	2	3				1	8
Longmuir [13,14]	3			19	1	25	12	60
Peja [25]	5			7	3	25		40
Vaccaro [38]			5					5
Bradley [39]	4		5					9
Ruttenberg [40]	10	2	3	9				24
Mathews [41]	3			2	1		1	7
Goldberg [42]	16					10		26
TOTAL	126	169	53	74	23	105	71	621

ToF: tetralogy of Fallot; TGA: transposition of the great arteries; L–R shunts: left to right shunts; and Prim HT: primary pulmonary hypertension.
Only the patients which completed the study are presented.
* Pulmonary hypertension present.

Table 3
Outcome regarding cardiac status, adverse outcomes and parameters of reported training programmes.

Reference	Test method cardiac status	Cardiac status and/or adverse outcome	Test method outcome parameter	Outcome
Müller [26]	–		MOT 4–6 (gives motor quotient)	Slight increase of motor quotient in whole group; significant increase in subgroup who had a less than normal motor quotient at baseline
Cordina [20]	Cardiac MR	Improvements in cardiac filling and cardiac output; as well as reduced dependence on respiration for blood return to the heart via IVC One transient ischemic event (not during training); no arrhythmia or other reported cardiac events	Strength test CPET, bicycle ramp-protocol, maximal test Total body DXA Calf MRS	Strength increased by 43 ± 7% Significant increase in $PeakVO_2$ (Δ 183 ± 31 ml/min) in training group; after 12-month detrained period there was a decrease of 0.5 l/min A significant increase of total body lean mass and non-dominant calf lean mass in training group (Δ1.94 ± 0.52 kg); after 12-month detrained period there was a decrease of 3.2 kg No significant change in calf MRS
Moalla [27]	–	All tests were well tolerated without major complaints or complication	Isokinetic dynometre (MVC and T_{lim}) NIRS over vastus lateralis muscle	MVC and T_{lim} significant increased in training group Significant improved use of oxygen and significantly faster reoxygenation in training group Both outcomes are highly correlated ($r = 0.95$)
Winter [17]	NT-proBNP	No significant changes One patient developed ventricular bigeminy in recovery phase of exercise test and was excluded from the study One patient sustained calf injury and discontinued the protocol for 2 weeks	CPET, bicycle ramp-protocol, maximal test QoL (SF-36 and CHD-TAAQOL)	Significant increase in $PeakVO_2$ and a significant improvement of OUES; both in the training group No changes in QoL
Martinez-Quintana [21]	NT-proBNP	No significant changes	6MWT Pedometer Hand grip strength Isometric strength of the quadriceps QoL (SF-12 V_2)	No significant change in either of the mentioned tests Although no endpoint, a perceived improvement of 1 NYHA class was noted in the training group
Dua [28]	ECG Echocardiogram	No mention of ECG or echocardiogram outcomes No death or adverse effects	CPET, treadmill standard Bruce protocol, maximal test QoL (PAQ, SF-12, SWLS and PSPP — scf) Accelerometer (actigraph and caltrac)	Median duration of treadmill exercise time significant increased All questionnaires used to assess QoL showed a significant increase Significant increase of mean moderate-to-vigorous-physical-activity; activity associated energy expenditure increased significantly
Amiard [22]	–	No trail was interrupted for angina, ST depression, arrhythmia or hypertension	CPET, bicycle ramp-protocol, maximal test	Non-significant improvement in aerobic capacity
Lichtman [43]	–	Remained in sinus rhythm	CPET, treadmill modified Bruce protocol, maximal test QoL (SF-36)	15% improvement in duration of treadmill exercise time; 26% increase of $PeakVO_2$ (ml/kg/min) 68% decrease in depression scale (CES-D in SF-36)
Singh [29]	–		CPET, bicycle ramp-protocol, maximal test	Significant improvement of $PeakVO_2$ (ml/kg/min) in training group; significant improvement of 1 and 3-min HR recovery in training group; $PeakVO_2$ and 3-min HR recovery was sustained during 4–10 month follow-up
Mcbride [30]	Telemetry during exercise Blood pressure measurements	2 seizures occurred, neither resulting in termination of the programme No adverse episodes of hypotension or significant arrhythmias occurred	–	–
Rhodes [15,16]	–	No rehabilitation-related complication occurred	CPET, bicycle ramp-protocol, maximal test	Significant improvement in $PeakVO_2$ and Peak Work rate, which is sustained during the follow-up period of 7 ± 2 months
Moalla and Maingourd [23]	–	No major complaint or complication	CPET, bicycle ramp-protocol, maximal test NIRS over respiratory muscles Pulmonary test	Significant improvement at Vth of VO_2, workload and HR, not significant at peak Significantly less deoxygenation in respiratory muscle indicating

				improvement of tissue oxygenation No significant changes in pulmonary test
Brassard [31]	–	–	CPET, bicycle ramp-protocol, maximal test Neuromuscular functioning	No change in $PeakVO_2$ Non-significant positive influence on neuromuscular function
Moalla and Gautier [18]	–	No symptoms or clinical complications occurred	6MWT CPET, bicycle ramp-protocol, maximal test	Significant improvement of walking distance in 6MWT Non-significant improvement of $PeakVO_2$ and PeakWL
Opocher [32]	–	–	CPET, treadmill Bruce protocol, maximal test	Significant improvement of METs' ratio, and $PeakVO_2$ after exclusion of non compliant subject
Therrien [19]	–	No death or morbid events Occasional premature ventricular and atrial beats	CPET, bicycle ramp-protocol, maximal test	Significant improvement of $PeakVO_2$
Minamisawa [33]	–	No adverse cardiovascular events occurred	CPET, bicycle ramp-protocol, maximal test	Significant improvement of $PeakVO_2$, PeakWL and exercise time
Fredriksen [24]	–	–	CPET, treadmill Oslo protocol, maximal test Activity monitor QoL (YSR and CBC)	Both (training and control) groups had significant increase in $PeakVO_2$, but not significant increase in training group corrected for weight Significant increase in activity in training group Marked increased social effect in both groups
Sklansky [34]	Echocardiography 24 h ECG	No significant echocardiac changes No significant changes in 24 h ECG registration	CPET, treadmill Bruce protocol, maximal test Single-stage submaximal exercise protocol	Significant improvement of treadmill time; significant decrease of submaximal HR and VO_2, indicating an improved exercise economy No significant training effect in submaximal exercise test
Balfour [35]	Patients at risk of dysrhythmias had a telemetry for 3 sessions	No mention of telemetry results	CPET, treadmill Bruce protocol, maximal test	Significant improvement of exercise time and $PeakVO_2$
Calzolari [37]	–	–	CPET, bicycle James-protocol, maximal test Submaximal exercise; treadmill	Non-significant improvement in exercise time and PeakWL Significant improvement of treadmill time at the submaximal exercise test
Tomassoni [36]	Single lead-ECG during each training session	No significant change ST depression	CPET, treadmill modified Bruce protocol, maximal test	Significant improvement of exercise time and cardiac output
Longmuir [13,14]	–	–	7 tests to assess cardiovascular endurance, strength, flexibility and coordination (based on the Canada Fitness Award test)	Significant improvement in the area of cardiovascular endurance in the compliant sport group; maintenance of the improvement during follow-up Significant improvement in the area of strength, flexibility and coordination in the compliant sport group; maintenance of the improvement during follow-up
Peja [25]	–	–	CPET; bicycle, submaximal test	Significant improvement in physical working capacity at HR 170 b/min
Vaccaro [38]	ECG at each training session	No significant change ST depression	CPET, treadmill maximal test	Increase in $PeakVO_2$ and treadmill time
Bradley [39]	Single lead-ECG during each training session	No complications	CPET, treadmill modified Bruce protocol, maximal test	Significant improvement of treadmill time and $PeakVO_2$
Ruttenberg [40]	–	–	CPET, treadmill Bruce protocol, maximal test	Significant improvement of $PeakVO_2$ and PeakWL in the group of left obstructive lesions; significant improvement of PeakWL in the TGA group
Mathews [41]	–	One patient with known ventricular arrhythmia died during eating	CPET, treadmill Balke protocol, maximal test 7 psychologic evaluations Lipid analysis	Three of the 4 subjects increased to normal values of $PeakVO_2$ Overall psychologic improvement Reduction in serum cholesterol
Goldberg [42]	–	–	CPET; bicycle, maximal test	Significant increase in PeakWL Significant decrease of submaximal HR and VO_2, indicating an improved exercise economy

MOT: motor developmental test; MR: magnetic resonance; IVC: inferior vena cava; CPET: cardiopulmonary exercise test; DXA: dual-energy X ray; MRS: muscle phosphorus spectroscopy; MVC: maximal voluntary contraction; T_{lim}: time to exhaustion (limit time); NIRS: near-infrared spectroscopy; OUES: oxygen uptake efficiency slope; QoL: quality of life; 6MWT: six minute walk test; NYHA: New York Heart Association; SF-36: short form 36 health survey; PAQ: physical activity (self-efficacy) questionnaire; SWLS: satisfaction with life scale; PSPP — scf: physical self-perception profile — short clinical form; CES-D: Centre for Epidemiologic Studies depression scale; YSR: youth self report; and CBC: child behaviour checklist.

[13–16]. In this review the 29 study populations are described and analysed.

4. Study design and patient population

The study population and design of the included studies are described in Table 1. A randomised study design was used 3 times [17–19], a cohort with a control group design 7 times [14,20–25], a cohort study design 18 times [15,26–42] and one study was a case report [43]. The age of the subjects in the study ranged from 4 to 45 years. Children were studied in 19 articles [13,15,16,18,22,24,25,27,29,30,32,34,36–40,42,44,45], 4 studies included children and young adults [33,35,41,46] and 6 studies included only adults [17,19–21,28,43].

The number of participants is shown in Fig. 1. The number of participants in the training group ranged from 1 to 55, with a median of 12. In 14 studies a matched control group of equal size was used [14,17–25,27,29,37,46]. Two studies included a control group of healthy volunteers, who participated in the same training programme [40,41]. Fredriksen et al. created a control group of patients who were interested in participating in the study, but did not want to be placed in the intervention group [24]. Singh et al. and Peja et al. created a control group of patients based on geographic location of the subjects; patients who lived away from the study location formed the control group [24].

Twenty-three studies (79% of all studies) reported their drop-out rate [13,16–21,24,27,28,30,32–37,39–43,45]. Nine (39%) of the studies had no drop-out at all [18,21,23,27,30,32,37,42,43]. Overall a median drop-out rate of 2 patients (6%) and a range of 0 to 36 participants were noted. The mean percentage of overall training participation, which was reported by 10 studies, was 82% (range 69–100%) [16,19,20,30,32,35,37,41–43]. An attendance rate of 100% was only reported by Lichtman et al. [43].

The reported duration of the training programmes varied between 6 and 52 weeks. Most studies used training programmes with a duration of 12 weeks (n = 13 studies) [16,18,19,21,26,27,29,35–39,45].

The number of training sessions reported ranged from 1 session per week up to daily training sessions. On average, the number of training sessions per week was 3 times. Five studies added voluntarily training sessions, consisting of the same aerobic exercise training activities used in the supervised training sessions, which were not registered [13,16,25,29,35]. Fredriksen et al. used two different training schemes: one home-based training scheme with 2 sessions a week, and one centre-based training scheme, for which the number of sessions was not stated [24]. Peja et al. divided their participants into groups based on functional status and created a training scheme per group [25].

The exercise time per session ranged between 5 and 60 min per session. Nine studies used a range of exercise duration [19,32,33,35,36,38–40,46]. Three studies did not state the duration of the sessions [14,24,43]. In one study time per session was incremental, lasting from 5 to 30 min per session [28]. One study only specified the duration for a proportion of the participants [25].

Training intensity was set at a percentage of peak heart rate in 12 studies, which was between 50 and 90% of peak heart rate (HR) [17,21,24,34–41,47]. One study had a set range of HR [25]. The ventilatory threshold level was used as intensity indicator in 5 studies [16,18,27,30,45]. Three studies used a percentage of $PeakVO_2$ [19,31,32]. Dyspnea threshold level was used in one study [22]; one other study used the rating of perceived exertion [43]. Peak workload as a guideline for physical exercise training was used in one study [42]; and one study based intensity on METS [28].

Seven studies used a home based physical exercise programme [17,18,22,23,27,28,42]. All home based studies used a monitoring system (heart rate monitor, email or telephone contact). Training was supervised in 10 studies [20,21,24,30,34,37,40,41,43,44]. All other studies used a combination of home-based training and supervised training [13,16,19,25,29,31–33,35,36,38,39].

Table 2 provides an overview of the different types of ConHD included in the studies. Patients with known arrhythmias and patients with significant residual obstructive lesions were not included in any of the studies.

Patients with Fontan circulation have been included as univentricular heart patients, regardless of their underlying pathology. Patients with transposition of the great arteries (TGA) corrected with either a Senning or Mustard operation were grouped together.

Ten studies included patients from a single diagnosis category [17,19,20,32–34,37,38,43,46]; 6 included Fontan patients [17,20,32,33,43,46], 3 included tetralogy of Fallot patients [19,34,37], and 1 included patients with TGA [38]. In total, 621 subjects were included, 169 (27%) patients with Fontan circulation, 126 (20%) ToF patients, 53 (9%) TGA patients, 74 (12%) with a left obstructive lesion, 23 (4%) with a right obstructive lesion, 105 (17%) with a left to right shunt and 71 (11%) subjects who had a heart defect which did not fit the previous categories.

5. Short-term effects of training programmes

Table 3 shows the methods used to assess the effects of the intervention.

5.1. Adverse events

Eighteen studies reported on the occurrence of adverse events. Thirteen did not report any adverse event [16,18,22,27,28,30,33,34,36,38,39,43,45]. In the other 5, an adverse event occurred [17,19,20,30,41]. In the study of Mathews, 1 patient with known ventricular arrhythmias died in circumstances not related to exercise [41]. One patient experienced a transient ischemic attack, 2 patients had seizures [30,20]. None of these events were related to exercise and/or training sessions. In 1 patient ventricular bigeminy was noted at the baseline ergometry test. This patient was excluded from the study, in concordance with the inclusion criteria [17]. One study mentioned occasional premature ventricular and atrial beats [19]. None of these patients were withdrawn from the studies. No one experienced sudden cardiac death during exercise.

5.2. Effects on the heart

Ten of the 29 studies measured the effect of an exercise programme on the heart. One study used cardiac MRI to assess ejection fraction, stroke volume and valvular regurgitation [20], 2 studies measured NT-proBNP [17,21], all other studies assessed potential ECG-changes as a result of physical exercise training. Improvements in ventricular filling and cardiac output were demonstrated using MRI. NT-proBNP did not change after training. There were no ECG changes due to physical exercise training.

Twenty-two studies found a statistically significant positive effect in their training group after the physical exercise training [13–20,23–29,32–40,42]. Sixteen studies of those involved only children (in total 19 studies with only children), 2 studies had a population of children and young adults (in total 4 studies with a mixed population) and 4 studies involved only adults (in total 6 studies with only adults).

Seven studies did not show any positive effect in their training group after the physical exercise training [21,22,30,38,41,43,46]. In the case of the study by McBride et al., the safety of an inpatient physical exercise training programme in paediatric patients awaiting heart transplantation while on inotropic support was the main aim, rather than the effects on fitness [30]. Six studies concluded that they were inadequate to assess physical exercise training effects, for reasons of small sample size and/or a training period that was too short [22,21,31,38,41,43]. Three of the studies that did not show any significant effect of the exercise intervention involved only children (from a total of 19 studies with only children) [22,30,38], 2 studies had a mixed population of children and young adults (from a total of 4 studies with a mixed population) [31,41] and 2 studies involved only adults (from 6 studies with adults only) [21,43].

5.3. Effects on exercise capacity

Twenty-four studies used a maximal exercise test to assess the training effect, either by graded cycle ergometry (13 studies) [15,17–20,22,23,25,29,31,33,37,42] or by treadmill [24,28,32,34–36, 38–41,43]. The Bruce protocol, modified or standard was used most frequently. In Fig. 2 the PeakVO$_2$ changes from those studies are shown. Mean baseline PeakVO$_2$ was 32.2 ml/kg/min. The mean increase after the training period (for 177 participants) in PeakVO$_2$ was 2.6 ml/kg/min. Twelve studies showed a statistically significant increase in PeakVO$_2$ in the training group [15,17,19,20,24,29, 32,33,35,38–40]. Two studies that did not show any significant change at PeakVO$_2$ showed a significant increase in VO$_2$ at ventilatory threshold [18,23], another two studies reported a significant decrease in sub maximal VO$_2$, indicating improved exercise economy [34,41]. Three studies did not report any significant increase in either PeakVO$_2$, nor in other VO$_2$ related parameters [22,31,43]. These 3 studies had a small sample size.

The six minute walk-test was used in 2 studies, once as an addition to the CPET, and once as the only assessment of the training effect [18,21]. Moalla et al. showed a significant improvement of walking distance [18] (in concordance with a significant increase in VO$_2$ at Vth), Martinez-Quintana did not show a significant improvement, as their study population was most likely too small [21].

5.4. Effects on muscle strength

Five studies reported on muscle-strength. Three reported a statistically significant increase in strength [14,20,27], Muller et al. reported an increase in the subset who had a less than normal motor quotient at baseline [26] and one reported no change [21], most likely due to the small study population.

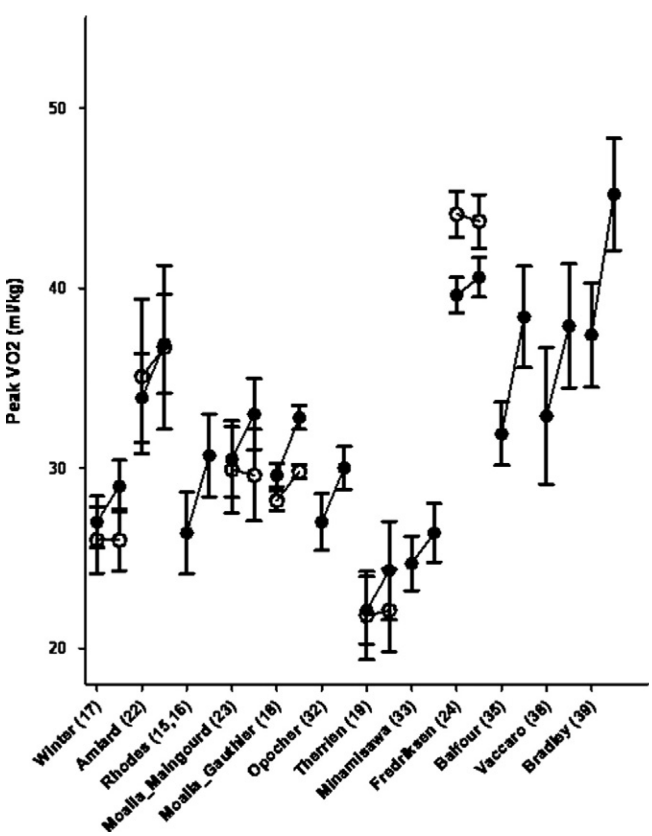

Fig. 2. Peak VO$_2$ values measured before and after the intervention. Closed rounds are the intervention groups, and were applicable; open rounds are the control groups.

5.5. Effects on activity level

Two studies measured change in activity level, and both found a significant increase in physical activity after training [24,28].

6. Long-term effects

Four studies re-assessed the training group after cessation of the training programme. Longmuir et al. retested the training group at 6 months post-training. The improvement in exercise capacity as measured directly after the training programme was sustained [13]. Rhodes et al. retested their training group after 5 to 9 months. They noted that the exercise function was sustained as well [15]. Singh et al. retested their training group subjects after 4 to 10 months. They noted a sustained improved 3-min heart rate recovery [29]. Mathews et al. noted a loss of training effect 6 months post training [41].

7. Discussion

The aim of the current review was to assess the negative or positive effects of physical exercise training programmes in children and young adults with ConHD. We found that most studies showed a significant positive effect of physical exercise training.

The majority of studies have been performed in paediatric populations. Sixteen out of the 19 studies in this age group showed a significant improvement of physical parameters. In the adult population 4 out of 6 studies showed the same effect. Four studies used a mixed population of children and adults. Significant improvement of physical parameters was noted in 2 of these studies. Since the success rates in the different age groups were not equal and the number of observations is relatively small we cannot draw firm conclusions on potential age related differences of physical exercise training programmes. Training effects in children with ConHD have been documented best [48].

Although some serious adverse events have been reported (in 4 out of 621 patients), from the description of these events it is unlikely that they were related to the exercise programme, or to the patients' underlying condition. None of the studies reported sudden cardiac death. Generally, there is little evidence that physical exercise training as described in the studies included in this review is not safe for patients with ConHD. It should be acknowledged that most studies excluded patients with sustained arrhythmias and severe obstruction to ventricular outflow. These are generally accepted contra-indications to perform physical exercise in patients with ConHD [49].

Few studies have examined the direct effects of physical exercise training on the heart or vasculature. Pro-arrhythmic ECG changes have not been observed, suggesting that exercise training does not increase the risk of arrhythmia in patients with ConHD. Only one study used an imaging technique (MRI) to assess cardiac effects and noted an improvement in ejection fraction and stroke volume. This is in line with findings in healthy individuals showing enhanced SV after a period of exercise training [50]. In patients with acquired heart disease positive cardiac outcomes have been reported. These benefits include improved left ventricular ejection fraction, favourable remodelling of the left ventricle, enhanced endothelial function and augmented regenerative capacity of circulating progenitor cells [5,51,52]. These effects have not been studied in patients with congenital heart disease in relation to exercise training. The relative lack of data on cardiac effects is remarkable and deserves further attention.

On average, physical exercise training resulted in a mean PeakVO$_2$ increase of 2.6 ml/kg/min, which is an average increase of ±8% of PeakVO$_2$, This is in line with the effects of exercise training in patients with acquired heart failure [5]. Maximal values are difficult to obtain, especially in the paediatric age group. Submaximal exercise measurements have been assessed in very limited number of studies. In the In the two studies that used the slope of the VE/VCO_2 slope relationship, no significant change was noted [17,31]. Winter et al. reported the oxygen uptake efficiency slope (OUES), which did not change significantly after training. Three studies reported VO_2 at ventilatory threshold, and demonstrated a significant increase after physical exercise training [15,18,23]. This suggests that oxygen delivery and consumption have improved and consequently the threshold for anaerobic metabolism has been shifted upward by exercise training.

Muscle strength was included in five studies that all used different methods. The studies that were not underpowered showed a significant increase in muscle strength [14,20,26,27]. Since muscle strength is an important parameter for functional daily life activities, the improved muscle strength will benefit the patient [53].

The two studies that measured activity levels found a significant increase in those levels after training. Although based on limited data, physical exercise training might get patients more active, and therefore less prone to a sedentary life with a reduced risk of cardiovascular disease associated with a sedentary life-style [3].

The differences in reported outcome measures such as oxygen uptake, activity level, muscle strength, submaximal performance, underline the lack of consensus on outcome measures for the physical exercise training in this population [48]. We recommend the establishment of a core-set of outcome measures to improve the benchmarking of different training protocols.

The large majority of the studies used dynamic submaximal exercise as the basis of the training programme. A different approach of was taken by Cordina et al. They used strength training to study cardiac changes and concluded that strength training, if performed without the Valsalva manoeuvre, is safe and may reduce the respiratory dependency in Fontan patients [20]. This questions the 'no strength training' dogma that is commonly applied in ConHD [48].

Failure to demonstrate training effects was commonly associated with a limited duration of the training programme and/or small sample sizes [22]. Over-all, the drop-out rate was low and participation in training was adequate. In general, significant positive effects of physical exercise training programmes were reported for those patients who trained for at least 8 weeks. The variation of duration of time per exercise session was limited, preventing clear conclusions on this factor. However, within the limits used (30–60 min), the duration of time per session did not seem to have an important influence on the general effect of the training programme. All studies used steady state designs. Interval training has been uncommon. Training intensity has been based on percentages of PeakHR, PeakVO_2 or ventilatory threshold. The available studies do not allow a conclusion on the most optimal training intensity. Training location had been considered an important factor in the sustainability of physical exercise training programmes. In the studies we evaluated, home-based programmes without direct supervision, supervised exercise in a centre, or a combination of both were used. There was no clear difference in outcomes depending on these strategies, therefore we concluded that both the centre based as well as the home base training programmes are feasible.

An important question is whether there could be differences in trainability between different diagnostic categories. Of the 6 studies that included only Fontan patients, 4 showed a significant effect [17,20,32,33]. The studies in Fontan patients that did not reach significant improvement most likely were underpowered due to small sample size [31,43]. In the 3 studies that included ToF patients exclusively, a significant effect on exercise capacity was noted in all [19,34,37]. Most studies included a range of different types of ConHD. Often this resulted in sample sizes that were too small to perform sub analyses per diagnostic category of ConHD. Therefore it remains unclear if a difference in trainability exists between different ConHD types. The extent of residual abnormalities may have an important impact on the exercise performance and thereby on the result of a physical exercise training programme. For instance, patients with a Fontan circulation may have reduced vasodilator response or chronotropic impairment [54]. Fontan patients with chronotropic incompetence may have more exercise limitation than those with chronotropic competence [30].

Long-term sustainability of training programmes is an important goal. Data in this review were limited. Only 4 studies described the long-term effects, measured up to 10 months after the exercise programme. Three out of these 4 reported a sustained effect of improvement in exercise capacity [13,16,29]. These results provide evidence for a long-term sustainability of improved exercise capacity. Consensus is lacking on optimal strategies to obtain sustained effects. This needs further study.

Reluctance of physicians to refer patients with ConHD to exercise programmes has been suggested to be among the reasons for low participation in exercise programmes of these patients. This reluctance may in part reflect the limited data on potential cardiac adverse effects of exercise in these patients. The effects of physical exercise training in ConHD with regard to fitness have been documented, as discussed in the current review. However, the lack of studies documenting the direct effect on the heart of such training programmes is striking.

Based on the findings of the current review, we recommend that future studies should be designed with at least 9 weeks of training supervised in person or by adequate monitoring tools. Future studies should have sufficient power to demonstrate effects of training schemes, in well-defined homogeneous study populations, with adequately randomised intervention and control groups. The design should allow measurements on exercise improvement, activity levels, and motor function, as well as on cardiac changes due to training. Furthermore, items that need to be addressed in future studies are proper outcome measures for the assessment of training programmes in congenital heart disease, the most adequate type of exercise, the duration and intensity of individual training sessions and of the entire training programme, the trainability of patients depending on underlying diagnosis, and the effects of the training location, particularly with regard to the long term sustainability of the effect on exercise performance.

In conclusion, most studies in this review showed that in children and young adults with ConHD exercise is safe and an improvement of fitness after a physical exercise training programme can be obtained, despite large variation in training schemes, the type of supervision of training and outcome measures. There is a lack of knowledge on the effect of exercise training on individual diagnostic categories and on the heart itself. This review supports the fact that physical exercise training should be a part of the congenital heart disease treatment as suggested previously in consensus reports [8,9].

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