Chapter

The Role of Cardiorespiratory Fitness in Children with Cardiovascular Risk

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Abstract

Cardiorespiratory fitness is an outcome of physical activity, enabling the transport of oxygen from the atmosphere to the mitochondria to perform physical work and therefore reflects the overall capacity of the cardiovascular and respiratory systems to perform the prolonged exercise. In recent decades, it has declined in the paediatric population. Cardiovascular fitness measurement has yet to be standardised in children but is a powerful marker of health in youth and is strongly associated with inflammation and inversely associated with cardiovascular risk factors, especially obesity. Notably, youth with low cardiorespiratory fitness levels have a higher risk of developing cardiovascular diseases during adulthood. Lowered cardiorespiratory fitness has been demonstrated most often in children with obesity and associated cardiovascular comorbidities, however, these can be associated with cardiorespiratory fitness independently to body mass index. The benefits of physical activity on health have been well demonstrated during growth and it should be encouraged in children with cardiovascular risk to prevent further reduction of cardiorespiratory fitness and the development of other comorbidities. Along with appropriate physical exercise and diet in childhood, breastfeeding in the first year of life is recommended.

Keywords: cardiorespiratory fitness, children, obesity, traditional cardiovascular risk, novel cardiovascular risk

1. Introduction

Cardiorespiratory fitness presents individuals’ ability to transport oxygen from the atmosphere to the mitochondria to perform physical work and therefore reflects the overall capacity of the cardiovascular and respiratory systems to perform prolonged exercise [1]. Cardiovascular fitness is therefore reflected in the ability of physical activity, which is critical in childhood as it lays the foundations for later physical activity – the base on which children can build more specific motor skills or develop movement patterns [2].

Epidemiologically, physical activity has been decreasing in the last decades [2], even more before the year of 2000, after which the trend stabilised with negligible changes [3] apart from COVID-19 epidemics, where cardiorespiratory fitness declined significantly [4, 5]. The decline in the last decades was more pronounced
Cardiorespiratory fitness was found to be higher in socially advantaged children [7].

Lower cardiorespiratory fitness is associated with low physical activity and increased fat mass. Increasing obesity in children is therefore strongly inversely associated with cardiorespiratory fitness and indicates reduced physical activity in the paediatric population in recent decades. Interestingly, fitness scores also decreased among lean children [8]. Association between low cardiorespiratory fitness and metabolic risk factors might therefore be only partially mediated through obesity [9]. Sedentary time also negatively affects cardiorespiratory fitness [10], which is independently linked to poor metabolic health [10]. Physical activity and sedentary time are clearly interrelated but a reciprocal relationship between them cannot be assumed [11]. Physical activity and training undoubtedly improve cardiovascular fitness with high-intensity interval training being more successful in enhancing cardiovascular fitness compared to moderate-intensity continuous training [12].

Cardiorespiratory fitness has been also associated with inflammatory biomarkers in children with a positive association with body fat. Similarly, the association between lifestyle behaviours, such as diet, physical activity and sedentary behaviour, and inflammation were found in the paediatric population [13].

Improved cardiorespiratory fitness was associated with the reduced inflammatory profile, independently of body composition and lifestyle behaviours [13]. Cardiorespiratory fitness and sports-related physical activity were also inversely associated with arterial stiffness in young adults [14].

Low cardiorespiratory fitness is strongly associated with the clustering of cardiovascular risk factors in children [15]. Evaluation and improvement of cardiorespiratory fitness in children with cardiovascular risk factors might be associated with improved health parameters in later life [1]. In this review, we present methods on how to evaluate cardiovascular fitness in children along with available data on cardiovascular fitness in children with some traditional and novel cardiovascular risk factors. Some specific strategies to improve cardiovascular fitness in children are also added.

2. Cardiorespiratory fitness in children: how to measure it?

Cardiorespiratory fitness was clearly associated with body mass index, fat mass, and metabolic syndrome development, however, other cardiovascular risk factors are not always convincing in the literature. Partly, this might be the result of the different evaluation of cardiovascular fitness in different studies [16]. The barriers to cardiovascular fitness assessment include the lack of standardisation in the test protocols, the health outcome being evaluated as well as the absence of evidence-based clinical cut points at these ages [17].

The most widely used indicator of cardiorespiratory fitness is the volume of oxygen that is consumed at maximal physical exertion (VO\textsubscript{2max}), measured from the respiratory gas exchange by indirect calorimetry [18]. It can be objectively and accurately measured through laboratory tests such as progressive run or cycle, however, these protocols require sophisticated equipment (run/cycle ergometer tests with respiratory gas analysis), the availability of trained technicians, making these tests expensive and time-consuming. Alternatively, field tests are more appropriate for universal screening and include a 550-m timed run/walk or “Maximal Multistage 20-m Shuttle Run Test” [18]. The latter was identified as
the most scalable and reliable field test, where VO$_{2\text{max}}$ can be predicted by special equations [19, 20]. For a field test to be valid it is required to accurately and reliably measure what it claims to measure, however, field-based tests usually suffer from low relative validity when compared to VO$_{2\text{max}}$ measurement and are producing conflicting results [18, 21]. Other similar screening tests are being developed, such as the 3-minute Kasch Pulse Recovery Test, where a reference range for the classification of cardiorespiratory fitness was developed on the basis of the age-specific percentile distribution of heart rate after exercise in 6- to 9- and 10- to 12-year-old children. The value of heart rate after exercise is considered an indicator of cardiorespiratory fitness [22].

Another obstacle in the cardiorespiratory fitness evaluation is the lack of age-specific cut-off points for increased cardiovascular risk. They were attempted to be set by a systematic review in children aged 8–19 years that determined that fitness levels below 42 and 35 mL/kg/min (VO$_{2\text{max}}$ measurement) for boys and girls, respectively, should raise a red flag. These cut-points identify children and adolescents who may benefit from primary and secondary cardiovascular prevention programming [17]. Similarly, a study using a 20-m Shuttle Run Test with VO$_{2\text{max}}$ prediction by estimation revealed cut-off points in 8- to 12-year-olds for obesity identified as 39 mL/kg/min and 41 mL/kg/min for girls and boys, respectively [23].

Recommendations for future research must include standardised measurements with standardised outcome assessments of cardiorespiratory fitness. For universal screening, a field test approach might be more appropriate, however, in children with cardiovascular risk, or suboptimal results in the field test, a more accurate approach might be more appropriate with cut-off points determined for gender and age.

3. Cardiorespiratory fitness in children with obesity

Children with obesity have lower cardiorespiratory fitness than normal-weight children [24], which is more pronounced in girls [25] and is commonly associated with reduced physical activity [26]. Body mass index also mediates the association between cardiorespiratory fitness and metabolic syndrome in schoolchildren. Higher levels of cardiorespiratory fitness are associated with lower cardiometabolic risk, particularly, when accompanied by weight reduction [27]. Lower cardiorespiratory fitness in children with obesity was associated with overall and abdominal fat mass, whereas both central and total obesity were lower in overweight and obese children with high cardiorespiratory fitness [28–30]. There is extensive evidence to support the fat-but-fit paradigm, which shows that cardiorespiratory fitness can counteract the adverse effects of obesity on cardiovascular risk factors. Unfit children with obesity had exaggerated systolic blood pressure at rest and during sympathetic activation, presumably coupled with higher cardiac output and cardiac oxygen demand [31]. Even from the molecular point of view, fit children with obesity or overweight had a distinct pattern of whole-blood gene expression [32]. Concerning the autonomic nervous system’s role, greater parasympathetic cardiac activity was associated with higher levels of cardiorespiratory fitness in both girls and boys, while the sympathetic-vagal balance was negatively related to maximal oxygen uptake in girls [33].

Additionally, in obesity, low-grade chronic inflammation and homeostatic stress produced mainly in adipocytes can result in abnormal adipokine secretion, which could be involved in the pathogenesis of lowered cardiorespiratory fitness. The secretion of adipokines is also influenced by physical fitness. It has been demonstrated that
4. Cardiorespiratory fitness in children with other traditional cardiovascular risk

4.1 Cardiorespiratory fitness in children with hypertension

Obesity-related hypertension is a problem on the rise with obesity epidemics. Cardiorespiratory fitness was associated with total and central obesity as well as hypertension [35, 36]. Systolic and diastolic blood pressure showed curvilinear relation with cardiorespiratory fitness along with waist circumference and the sum of skinfolds [37]. However, regardless of obesity, cardiorespiratory fitness in children has been associated with other metabolic risk factors and future health. Teenagers with low cardiorespiratory fitness were more likely to develop hypertension in adulthood, even among participants with a normal body mass index [24]. Children who are fit and participate regularly in sports outside school hours are less likely to be hypertensive [38]. Long-term low levels of cardiorespiratory fitness exhibited the highest levels of systolic blood pressure [39]. The combination of a family history of hypertension and cardiorespiratory fitness also showed a clear association with the increased risk of hypertension [40]. Interestingly, some studies set a different perspective on cardiorespiratory fitness and hypertension, somehow contradicting the above-mentioned associations. In one of them, physical activity was not associated with systolic blood pressure independently of adiposity, but there was a small independent association only with diastolic blood pressure [41]. Another study demonstrated that adolescents with overweight or obesity have a higher prevalence of higher blood pressure, regardless of cardiorespiratory fitness, suggesting that maintaining a normal body mass index protects against less favourable blood pressure [42]. Anyway, a study published two decades ago demonstrated that the level of cardiorespiratory fitness did not seem to be an important correlate of blood pressure variation across age groups and gender in schoolchildren [43].

4.2 Cardiorespiratory fitness in children with dyslipidaemia

Abnormal lipid profile is commonly known as a cardiovascular risk factor, sometimes associated with obesity, but in children, it can be the consequence of genetic defect leading to familial hypercholesterolemia also in lean children [44]. However, specific studies regarding familial hypercholesterolemia and cardiorespiratory fitness are lacking in the paediatric population. Overall, evidence supports an inverse association between cardiorespiratory fitness and dyslipidaemia with expected improvements in high-density lipoprotein cholesterol with exercise, which is the most consistent finding. The findings regarding the effects of exercise training on other lipid components have been variable, with both positive and null results, but in general demonstrate a reduction of total cholesterol and triglycerides with exercise training [45, 46]. Future studies in the paediatric population are needed to clarify the association between cardiorespiratory fitness change and dyslipidaemia [45].

4.3 Cardiorespiratory fitness in children with diabetes mellitus type 1 or type 2

Lower cardiorespiratory fitness, strength, and higher central adiposity were also highly predictive of higher levels of insulin resistance in children and adolescents.
without diabetes mellitus [47], however, at least in part, are mediated through obesity [48]. Nevertheless, increased muscle strength and cardiorespiratory fitness were associated with decreased insulin resistance and improved $\beta$-cell function among young in population studies [49, 50]. Cardiorespiratory fitness and muscular fitness in children are not only important in childhood but it was proven that they were inversely associated with measures of fasting insulin, insulin resistance, and $\beta$-cell function in adulthood [51].

In children with already developed diabetes mellitus, cardiorespiratory fitness might play an even more pivotal role. Independently of obesity, there was a significant inverse relationship between cardiorespiratory fitness and lipid profile components and systolic blood pressure in children with poorly controlled type 1 diabetes mellitus, indicating a favourable effect of increased cardiorespiratory fitness [52]. Additionally, youth with diabetes mellitus type 1 who are physically active, tend to have lower glycated haemoglobin and reduced insulin needs. Also, activity in adolescents at-risk for diabetes mellitus type 2 improves various measures of metabolism and body composition [53]. In children with diabetes mellitus type 2, lower levels of cardiorespiratory fitness were observed mostly due to physical inactivity [54]. People with diabetes mellitus type 2 have reduced cardiorespiratory fitness compared to healthy controls, with an association to increased cardiovascular morbidity and mortality. The mechanisms of lower cardiorespiratory fitness in children with diabetes mellitus type 2 are multifaceted and involve interrelated defects in insulin action, mitochondrial dysfunction, skeletal muscle microvasculature, and cardiac dysfunction [55]. In youth with diabetes mellitus type 2, left ventricular size is clearly related to physical fitness, which might counteract adverse effects of poor glycaemic control and, at least according to the study, right ventricular function [56]. Regular physical activity is an important component in the management of both diabetes mellitus type 1 and type 2, as it has the potential to improve glycaemic control, delay cardiovascular complications, and increase overall well-being [57].

5. Cardiorespiratory fitness in children with novel cardiovascular risk

5.1 Cardiorespiratory fitness in children with chronic kidney disease

Children with chronic kidney disease have lower cardiorespiratory fitness due to various reasons, one of the most important is reduced physical activity and increased sedentary lifestyle mainly due to the renal replacement therapy requirements (e.g. haemodialysis) [58]. Additionally, chronic kidney disease is associated with anaemia, effects of chronic uraemia, and metabolic acidosis on the heart and skeletal muscle, all contributing significantly to reduce physical activity [59]. Paediatric patients with chronic kidney disease are therefore significantly physically inactive, with less than 10% of the non-school time being physically active [60]. Additionally, children after kidney transplantation significantly gained fat weight [60, 61]. One of the reasons after transplantation might also be related to sirolimus effects on skeletal muscle [61]. Reduced cardiorespiratory fitness was strongly associated with the clustering of cardiovascular risk factors in these children [62].

Studies suggest that regular and early implementation of both aerobic and resistance exercise programs in persons with chronic kidney disease have positive effects on muscle function, exercise tolerance, and quality of life [59]. In children with a
successful renal transplant, a weekly physical exercise of 3–5 hours significantly improved cardiorespiratory fitness and left ventricular mass [63].

In children with a congenital single kidney, physical activity improved aerobic capacity and exercise tolerance without increasing the risks of cardiovascular accidents [64], however, in the patients contact sports might be discouraged due to the increased risk of sport-related injury.

5.2 Cardiorespiratory fitness in children born prematurely

Children and also later adults, born prematurely, are likely to have poorer cardiorespiratory fitness, however, according to some studies, the poor cardiorespiratory outcome of a child born prematurely is not firmly established [65, 66]. In adults, exercise capacity was only modestly reduced and frequently with values within a normal range and was consistent with self-reported exercise capacity [67]. In addition, in children with abnormal lung function and structure, this did not impact the aerobic exercise capacity of preterm children at school age [68]. On the contrary, Welsh et al. demonstrated a significant reduction in peak oxygen consumption among prematurely born children but with no difference in physical activity [69]. Some subgroups of premature-born individuals might be at increased risk for reduced cardiorespiratory fitness, especially those with lower muscular fitness, which was more common among premature-born young adults [70]. Lowered muscle strength is associated also with neuromotor sequelae of premature birth [71]. Another risk factor for reduced exercise capacity is also a decreased ventricular size and mass that might be a consequence of prematurity [72]. Impaired heart rate recovery after maximal exercise might also play a role in poor cardiorespiratory fitness in some suggesting an impaired development of autonomic nervous function after preterm labour [73].

Babies, born prematurely, are a diverse group of patients with complications that depend on several factors, such as gestational age, associated comorbidities, prenatal factors, postnatal care, etc. Therefore, the studies are diverse and might contradict each other because the effect of premature birth depends on so many other factors. Anyway, children born prematurely do have a risk for lowered cardiorespiratory fitness and regular physical intervention is believed to produce better outcomes [65, 71].

5.3 Cardiorespiratory fitness in children with congenital heart disease

Congenital heart disease may in a variety of ways adversely affect hemodynamic responses, usually produced during exercises, such as increased heart rate, preload, and heart contractility with decreased systemic vascular resistance and pulmonary vascular resistance [74]. Therefore, the consequences of cardiorespiratory fitness depend on the congenital defect itself and a proper evaluation is of pivotal importance to evaluate cardiac rehabilitation. Historically, children with congenital heart disease have been restricted from exercise, contributing to a sedentary lifestyle as well as increased cardiovascular risk factors. Given the large benefits and small risks of exercise in this population, guidelines have recently shifted towards exercise promotion [75]. In children, several tests to evaluate cardiorespiratory fitness might be used [74], however, the 6-minute walk test is quite common and was found to be a useful and reliable tool in the assessment and follow-up of functional capacity during rehabilitation programs [76]. Furthermore, exercise training is safe and beneficial for the vast majority of adults with congenital heart disease following appropriate screening [77, 78].
Exercise recommendations should be individualised based on functional parameters using a structured methodology to approach the evaluation, risk classification, and prescriptions of exercise and physical activity [75]. Participation in aerobic exercise significantly increased the quality of life in children with congenital heart disease [79].

### 6. Cardiorespiratory fitness, sleep and psychosocial well-being

Sleeping quality was also associated with cardiorespiratory fitness, not necessarily in children with high body mass index, as might be expected. Girls who were classified as fit were more likely to report better sleep quality compared to their unfit peers. Poor sleep quality was associated with lower cardiorespiratory fitness with no significant association with body mass index [80].

Not only obesity reduction, but improved cardiorespiratory fitness also positively affects psychosocial well-being, leading to improved self-esteem and reduced stress, further reducing cardiovascular risk. Cognitive function and cardiorespiratory fitness correlate significantly and are predictors of psychological well-being among school-aged children. In addition, students with a higher level of psychological well-being showed a higher cardiorespiratory fitness, concentration performance, and attention accuracy [81]. Cardiorespiratory fitness also had a small protective effect against developing depression [82]. Similarly, it was found that stress and depression can affect an individual's level of physical activity and fitness, which may place them at risk of developing cardiovascular disease, confirming the role of increased physical activity in improving depression and reducing depression-related stress to improve cardiovascular risk [83].

### 7. Strategies to improve cardiorespiratory fitness in children

Addressing cardiovascular fitness in children and adolescents could reduce future adiposity, improve other cardiovascular risk factors and thus be an important factor in improving health [16]. The main strategies for reducing cardiovascular risk and obesity remain physical exercise with a reduced sedentary lifestyle and an appropriate diet. Promoting health-related cardiorespiratory fitness in physical education proved to be an important contributor to improving cardiorespiratory fitness in children. Intensity, age, and weight status importantly affect cardiorespiratory fitness [84]. In children with obesity, regular exercise is even more important, and may not need to be vigorous; recreational programs are also effective and may encourage children to participate in physical activity and limit initial dropout. Three-month training programs in children with obesity led to decreased body mass index, waist circumference, decreased fat mass, blood glucose, homeostasis model assessment for insulin resistance, triglycerides, and systolic pressure before and after exercise [85].

A healthier diet in preschool and schoolchildren also led to lower adiposity levels, lower waist circumference, and increased cardiorespiratory fitness, making it a relevant modifiable factor in obesity management [86, 87].

The management of the whole family is of utmost importance because a parent's effect can have a significant impact on children's willingness and motivation to change their lifestyle [88]. Breastfeeding has also been positively associated with cardiorespiratory fitness, where breastfeeding for more than 6 months proved to have positive
effects on cardiorespiratory fitness. Therefore, early nutrition may be a predictor for adolescence physical health and is of special importance to promoting healthier lifestyle in children as it is associated with higher cardiorespiratory fitness [89].

Intervention strategies aiming to reduce obesity and improve cardiorespiratory fitness in childhood might contribute to the prevention of metabolic syndrome in adulthood [90]. The process is schematically presented in Figure 1.

8. Conclusions

Cardiorespiratory fitness is declining in the paediatric population and is closely associated with increased cardiovascular risk. In children already having a cardiovascular risk factor present, it is important to determine cardiorespiratory fitness and if it is decreased, prompt physical intervention is warranted. Further research is needed to establish a standardised protocol of its measurement. Interventions include increased and customized physical activity along with a healthy diet. In children, breastfeeding could present an additional preventive factor.

Conflict of interest

The authors declare no conflict of interest.
The Role of Cardiorespiratory Fitness in Children with Cardiovascular Risk
DOI: http://dx.doi.org/10.5772/intechopen.104701

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