The Associations of cardiorespiratory fitness, adiposity, and sports participation with arterial stiffness in youth with chronic diseases or physical disabilities

Running head: Fitness, adiposity, and arterial stiffness

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Abstract

Background. The evidence on the associations of cardiorespiratory fitness, body adiposity, and sports participation with arterial stiffness in children and adolescents with chronic diseases or physical disabilities is limited.

Design. Cross-sectional.

Methods. Altogether 140 children and adolescents with chronic diseases or physical disabilities participated in the study. Cardiorespiratory fitness was assessed using maximal exercise test with respiratory gas analyses either using shuttle run, shuttle ride, or cycle ergometer test. Cardiorespiratory fitness was defined as peak oxygen uptake ($\dot{V}O_{2peak}$) by body weight or fat free mass (FFM). Body adiposity was assessed using waist circumference, body mass index standard-deviation score (BMI-SDS), and body fat percentage. Sports participation was assessed by a questionnaire. Aortic pulse wave velocity PWV (PWVao) and augmentation index (AIX%) were assessed by a non-invasive oscillometric tonometry device.

Results. $\dot{V}O_{2peak}$/body weight (standardized regression coefficient β=-0.222, 95% CI=-0.386 to -0.059, *P*=0.002) and VO_{2peak}/FFM (β=-0.173, 95% CI=-0.329 to -0.017, *P*=0.030) were inversely and waist circumference directly (β=0.245, 95% confidence interval (CI)=0.093 to 0.414, *P*=0.002) associated with PWVao. However, the associations of the measures of cardiorespiratory fitness with PWVao were attenuated after further adjustment for waist circumference. A higher waist circumference (β=-0.215, 95% CI=-0.381 to -0.049, *P*=0.012) and a higher BMI-SDS (β=0.218, 95% CI=-0.382 to -0.054, *P*=0.010) were related to lower AIX%.

Conclusions. Poor cardiorespiratory fitness and higher waist circumference were associated with increased arterial stiffness in children and adolescents with chronic diseases and physical disabilities. The association between cardiorespiratory fitness and arterial stiffness was partly explained by waist circumference.

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Key words: Youth, arterial stiffness, exercise, cardiorespiratory fitness, obesity, chronic disease

Introduction

Arteriosclerotic cardiovascular diseases are one of the leading causes of morbidity and mortality and the costs related to arteriosclerosis demonstrate a considerable economic burden[1]. Arterial stiffness and endothelial dysfunction are the first signs of arteriosclerosis and they have been established already in children and adolescents[2,3]. In adults, increased arterial stiffness has been found to predict subsequent clinical cardiovascular events[4]. Therefore, early identification of children and adolescents with increased arterial stiffness is of importance in order to prevent arteriosclerotic cardiovascular diseases in later years[1].

Poor cardiorespiratory fitness has been associated with higher carotid and femoral artery stiffness and aortic intima media thickness (IMT) and elasticity in adolescents[5,6]. Better cardiorespiratory fitness in adolescence also has been linked to lower femoral artery stiffness and carotid IMT at the age of 36[7]. Furthermore, obesity has been consistently related to stiffer carotid and aortic arteries among youth[8]. Higher levels of habitual physical activity have been associated with lower arterial stiffness, lower aortic IMT, and improved endothelial function in children and adolescents in some[9–11], but not all studies[12–15]. Furthermore, constantly high levels of vigorous physical activity between ages 13 and 36 have been linked to lower arterial stiffness at the age of 36 years[16]. Finally, the results of some previous studies suggest that exercise training has favorable effects on flow-mediated dilation as a marker of endothelial function in overweight and obese children and adolescents[17].

Children and adolescents with chronic diseases or physical disabilities may have an increased risk of arteriosclerosis[18]. The evidence suggest that children and adolescents with chronic diseases or physical disabilities have lower cardiorespiratory fitness[19], higher prevalence of overweight and obesity[19,20], lower levels of physical activity[20,21], and they participate less often in organized sports[20], than their apparently healthy or normally developing peers. Children and adolescents with chronic disease or disabilities may also have increased arterial stiffness[22]. Studies among adults also suggest that arterial stiffness is particularly important marker of subsequent cardiovascular morbidity and mortality among those with chronic cardiovascular or metabolic diseases[4]. However, one small study found no differences in arterial structure and function between children with cerebral palsy (CP) and normally developing children with similar levels of physical activity and body adiposity[23]. Nevertheless, there are no studies on the associations of cardiorespiratory fitness, body adiposity, and sports participation with arterial stiffness in a large sample of children and adolescents with chronic diseases or physical disabilities.

The aim of the present study was to investigate the associations of cardiorespiratory fitness, body adiposity, and sports participation with arterial stiffness in children and adolescents with chronic diseases or physical disabilities. We also studied if there are thresholds for cardiorespiratory fitness and the measures of body adiposity that are associated with increased arterial stiffness.

Methods

Participants

The present analyses are based on the data from the Health in Adapted Youth Sports (HAYS) Study and the Sport-2-Stay-Fit (S2SF) Study. These studies are designed to investigate the associations of sports participation and exercise training with physical fitness, physical activity, body adiposity, cognition, cardiovascular health, and quality of life in children and adolescents with chronic diseases or physical disabilities. The study designs are published in detail elsewhere[24,25].

The children and adolescents for the HAYS Study and S2SF Study were recruited in the Netherlands among different patients' associations, pediatric physical therapy practices, Wilhelmina Children's Hospital in Utrecht, De Hoogstraat Rehabilitation Center in Utrecht, Fitkids practices, Schools for special education, and adapted sports organizations. The inclusion criteria for the HAYS Study and the S2SF Study was that participants had to understand the Dutch language, understand simple instructions, and be able to perform physical fitness tests. All ambulatory children and adolescents and wheelchair users were eligible to participate. Children and adolescents using an electric wheelchair, having a progressive disease, who participated in other research projects, or who had contra-indications for performing a maximal exercise test were excluded.

Ethical approval

The study protocols were approved by the Medical Ethics Committee of the University Medical Center Utrecht, the Netherlands (METC number: 14-332/c and 14-118/m). All participants and the parents of participants under 18-years-of-age provided their informed written consent. Studies were conducted in accordance to the Helsinki declaration.

Assessment of cardiorespiratory fitness

Peak oxygen uptake ($\dot{V}O_{2peak}$) as a measure of cardiorespiratory fitness was assessed either by an adapted 10-meter incremental shuttle run test, by a 10-meter incremental shuttle ride test, or by an incremental cardiopulmonary exercise test on an electronically braked Ergoline cycle ergometer (Ergoselect 200 K, Ergoline, Bitz, Germany)[24]. The test modality was based on the evaluation of children's ambulatory ability, mode of daily locomotion, type of sports, and safety issues. All children with a congenital cardiopulmonary disease underwent an incremental cardiopulmonary exercise test with continuous electrocardiography (ECG) monitoring on a cycle ergometer. Participants who were able to walk or run performed an incremental shuttle run test and wheelchair users performed a shuttle ride test. Altogether 64% of the participants performed a shuttle run test, 11% a shuttle ride test, and 24% a cycle ergometer test. All the test procedures have been described in detail previously[24].

Respiratory gases were collected using pediatric masks (Hans–Rudolph, Shawnee, Kansas, USA) during the test by a calibrated metabolic cart (Cortex Metamax, Samcon bvba, Melle, Belgium). Regardless of testing modality, respiratory gases were measured directly by the breath-by-breath method from the 3-min resting steady-state period to the post-exercise rest and were averaged over consecutive 10-s periods.

Children and adolescents were verbally encouraged to exercise until voluntary exhaustion. The exercise test was considered maximal, if the subjective and objective criteria indicated maximal effort and maximal cardiorespiratory capacity (i.e. flushing, sweating, heart rate >180, RER >1.0, or plateau of $\dot{V}O_2$). Cardiorespiratory fitness was defined as $\dot{V}O_{2peak}$ per body weight and $\dot{V}O_{2peak}$ per kg fat free mass (FFM).

Assessment of body size and body adiposity

Body size and composition were measured after emptying the bladder. Body height was measured by stadiometer (Seca, Hamburg, Germany) in ambulant participants. Among participants using wheelchair the body height was measured in a supine position using a measuring tape. In case of spasticity of the lower limbs, arm span width was measured to the nearest centimeter from middle fingertip to fingertip. Body weight was measured by standard scale (Seca, Hamburg, Germany). Participants who used a wheelchair and who were not able to stand on a scale were measured using a wheelchair scale (Stimag B.V., Lisse, the Netherlands). Body mass index (BMI) was calculated as body weight (kg) / body height $(m)^2$ for ambulant participants and as body weight (kg) / the arm span length. We used arm span adjustment of × 0.95 and × 0.90 for participants with central neurological disorders in mid-lumbar lesions and high lumbar/thoracic lesions, respectively[26]. Waist circumference was measured by an unstretchable measuring tape at the level of the navel. BMI-standard deviation score (SDS) and waist circumference-SDS were computed using national reference values[27]. Body fat percentage and FFM were measured by bioelectrical impedance analyses using Bodystat Quadscan 4000 device (EuroMedix, Leuven, Belgium).

Assessment of sports participation

To allow a comparison between children and adolescents with chronic diseases or physical disabilities who participated in organized sports and those without regular sports participation we recruited sports participants from a broad range of participation in sports including recreational level as well as high level competitive sports[24]. The study participants reported how often they participated in organized sports on a questionnaire. In the present study, we defined regular sports participation as any involvement in organized sports at least 2 times per week.

Assessment of arterial stiffness

Aortic PWV (PWVao), as a measure of arterial stiffness, and augmentation index (AIX%), as measure of peripheral arterial tone, were assessed by non-invasive oscillometric tonometry device (Arteriograph, TensioMed Ltd, Budapest, Hungary) from the right arm. PWVao and AIX% derived from the Arteriograph analyses have been validated against an invasive method in adults. The correlation of invasively assessed PWVao and AIX% to PWVao and AIX% measured by the Arteriograph has been found to be strong ($r>0.90$) with a reasonable agreement between oscillometric tonometry and invasive methods[28]. Before the measurement, participants were asked to rest in a supine position for 10 minutes. Age and sex-specific SDS-norm values for PWVao and AIX% were calculated based on the data of over a 4500 Caucasian children and adolescents[29,30]. A higher PWVao indicates a higher aortic stiffness and a higher AIX% indicates a higher peripheral arterial tone.

Systolic blood pressure was also assessed by the Arteriograph device (TensioMed Ltd, Budabest, Hungary) in a supine position after ten-minute rest.

Statistical methods

Basic characteristics between boys and girls were compared using the Student´s t-test, the Mann-Whitney U-test, or the Chi Square-test. The associations of cardiorespiratory fitness and body adiposity as independent variables with PWVao and AIX% as dependent variables were studied using linear regression analyses adjusted for age and sex. The differences in PWVao and AIX% between sport participants and non-sport participants were investigated using general linear models (GLM) adjusted for age and sex. The data on the associations of cardiorespiratory fitness, body adiposity, and sports participation with PWVao and AIX% were also mutually adjusted.

All data were additionally controlled for systolic blood pressure, the mode of exercise testing, and diagnose (cardiovascular disease vs. other).

Receiver operating characteristics (ROC) curves were used to investigate the optimal cutoff for VO_{2peak}, waist circumference, BMI-SDS, and body fat percentage to identify children and adolescents at or over +1SD of PWVao and AIX% reference values[29,30]. The area under the curve (AUC) is considered a measure of the effectiveness of the predictor variable to correctly identify children and adolescents at or above +1SD of PWVao and AIX% (sensitivity) and to correctly identify participants (specificity) below +1SD of PWVao and AIX%. An AUC of 1 represents the ability to perfectly identify children and adolescents at or above +1SD of PWVao and AIX% from other participants, whereas an AUC of 0.5 indicates no greater predictive ability than chance alone.

The optimal cutoff was determined by the Youden index[31], which is the maximum value of J that is computed as: sensitivity + specificity - 1.

The effect modification of sex was investigated by general linear models (GLM). Because we found no statistically significant sex-interactions between the measures of cardiorespiratory fitness and body adiposity and the outcome variables, we performed all analyses with data of boys and girls combined.

Student´s t-test, the Mann-Whitney U-test, the Chi Square-test, GLM analyses, and the linear regression analyses were performed using the SPSS Statistics, Version 23.0 (IBM Corp., Armonk, NY, USA). The ROC curve analyses were performed using MedCalc Statistical Software, Version

16.1 (MedCalc Software bvba, Ostend, Belgium). A *P*-value of < 0.05 was considered as statistically significant.

Results

Descriptive characteristics

Complete data on variables used in the present analyses were available for 140 children and adolescents with chronic diseases or physical disabilities (86 boys, 54 girls). Children and adolescents who were excluded (N=37, 20 boys, 17 girls) from the present analyses because of the missing data did not differ from those who were included in waist circumference or BMI-SDS. Children and adolescents who were included in the present analyses were slightly older than those who were excluded from the present analyses (*P*=0.029).

Among the included children and adolescents, boys were taller, had a lower body fat percentage, higher $\dot{V}O_{2peak}$, and a lower AIX% than girls (Table 1). Seventy-six (56%) of the included children and adolescents participated in sports. Altogether 17 children and adolescents had a cardiovascular disease, four had a pulmonary disease, 10 had a metabolic disease, 11 had a musculoskeletal/orthopedic disability, 82 had a neuromuscular disease/disability, six had an immunological/hematological disease, three had cancer, and seven had epilepsy (Table 1). There were no age-differences among the children and adolescents in different diagnosis groups (*P*=0.682).

Table 1. Descriptive characteristics.

	All	Boys (N=84)	Girls (N=56)	*P*-value
Age (years)	14.3 (2.7)	14.1 (2.7)	14.7 (2.9)	0.078
Body height (cm)	160 (14.3)	162.7 (15.9)	157.9 (10.9)	0.033
Body weight (kg)	54.8 (16.6)	56.7 (18.4)	51.7 (12.7)	0.059
Body mass index* (kg/m^2)	20.0 (5.2)	20.2 (5.6)	19.7 (5.1)	0.681
Body mass index-standard deviation score	0.68 (1.3)	0.83 (1.3)	0.43 (1.3)	0.078
Prevalence of overweight (%)	39.3	43	33.3	0.253
Waist circumference (cm)	75.7 (13.3)	75.6 (14.2)	75.9 (12.1)	0.888
Waist circumference- standard deviation score	0.8 (1.3)	0.7 (1.5)	1.1 (1.1)	0.062
Body fat percentage (%)	23.9 (9.7)	21.2 (9.4)	28.1 (8.7)	<0.001
Peak oxygen uptake (L/min)	2.1 (1.0)	2.5 (0.9)	1.8 (0.4)	<0.001
Peak oxygen uptake (ml/kg/min)*	40.0 (15.0)	44.0 (15.0)	36.0 (11.0)	<0.001
Peak oxygen uptake (ml/FFM/min)*	52.9 (13.7)	56.5 (14.8)	51.1 (8.1)	<0.001
Aortic pulse wave velocity (m/s)*	5.8 (1.3)	5.8 (1.2)	5.8 (1.1)	0.098
Aortic pulse wave velocity-standard deviation score*	-0.17 (1.71)	-0.21 (1.7)	-0.04 (1.7)	0.189
Aortic augmentation index (%)*	9.0 (10.4)	7.7 (11.4)	10.1 (10.3)	0.005
Aortic augmentation index (%)-standard deviation score *	0.19 (1.23)	0.17 (1.2)	0.25 (1.2)	0.245

FFM, fat free mass. The data are mean (standard deviations), median (interquartile range*), or percentages and the *P*-values from the *t*-test for independent samples for continuous variables with normal distribution and Mann-Whitney U-test for continuous variables with skewed distribution, or Chi-square for prevalence of overweight.

Associations of cardiorespiratory fitness body adiposity, and sports participation with arterial stiffness

$\dot{V}O_{2peak}$ per body weight and $\dot{V}O_{2peak}$ per FFM were inversely and waist circumference directly associated with PWVao after adjustment for age and sex (Table 2). However, the relationship of $\dot{V}O_{2peak}$ per body weight (β=-0.133, 95% CI = -0.315 to 0.050, P=0.152) and $\dot{V}O_{2peak}$ per FFM (β=-

0.137, 95% CI = -0.291 to 0.017, P=0.082) to PWVao were no longer statistically significant after further adjustment for waist circumference. Additional adjustment for systolic blood pressure, the mode of exercise testing, or diagnose had no effect on these associations (data not shown).

Table 2. Associations of cardiorespiratory fitness and body adiposity with arterial stiffness in 140 children and adolescents with chronic diseases or physical disabilities.

	Aortic pulse wave velocity (m/s)			Aortic augmentation index (%)		
	B	95% CI	*P*	B	95% CI	*P*
Peak oxygen uptake (mL/kg/min)	-0.222	-0.386 to -0.059	0.008	-0.100	-0.271 to 0.070	0.247
Peak oxygen uptake (mL/fat free mass/min)	-0.173	-0.329 to -0.017	0.030	-0.120	-0.281 to 0.041	0.142
Waist circumference (cm)	0.254	0.093 to 0.414	0.002	-0.215	-0.381 to -0.049	0.012
Body mass index-standard deviation score	0.141	-0.026 to 0.307	0.097	-0.218	-0.382 to -0.054	0.010
Body fat percentage (%)	0.036	-0.127 to 0.198	0.664	0.016	-0.150 to 0.183	0.847

The data are standardized regression coefficients and their 95% confidence intervals adjusted for age and sex.

Waist circumference and BMI-SDS were inversely associated with AIX% after adjustment for age and sex. Further adjustment for the measures of cardiorespiratory fitness or sports participation had no effect on these associations (data not shown). However, further adjustment for systolic blood pressure slightly attenuated the association between waist circumference and AIX% (β=-0.166, 95% CI = -0.343 to 0.010, P=0.064). Additional adjustment for the mode of exercise testing, or diagnose had no effect on these associations (data not shown).

Sports participation was not associated with PWVao or AIX% after adjustment for age and sex (P>0.40). The associations of cardiorespiratory fitness, body adiposity, sports participation with PWVao and AIX% remained similar when PWVao-SDS and AIX%-SDS were used as outcome measures or waist circumference-SDS was used as an independent variable (data not shown).

Ability of cardiorespiratory fitness and body adiposity to identify children and adolescents with increased arterial stiffness

The ROC curve analyses revealed that the optimal cutoff for waist circumference to identify children and adolescents ≥1SD of PWV-SDS was >73cm (95% CI = 66 to 78) with a sensitivity of 81%, a specificity of 53%, and the Youden index of 0.3386 (Figure 1.). The corresponding cutoff for waist circumference-SDS was >-0.05 units (95% CI = -0.09 to -0.02) with a sensitivity of 81%, a specificity 54%, and the Youden index of 0.3477. The optimal cutoff for $\dot{V}O_{2peak}$ per body weight was <35 ml/kg/min (95% CI 27 to 40) with a sensitivity of 48%, a specificity of 76%, and the Youden index of 0.2453. These analyses indicated that children and adolescents with a higher waist circumference and a lower $\dot{V}O_{2peak}$ per body weight were more likely to have increased arterial stiffness.

The optimal cutoff for $\dot{V}O_{2peak}$ per FFM to identify children and adolescents ≥1SD of AIX%-SDS was <51 ml/kg FFM/min (95% CI 46 to 66) with a sensitivity of 64%, a specificity of 66%, and the Youden index of 0.3036 suggesting that children and adolescents with poorer cardiorespiratory fitness had increased AIX% compared to those with better cardiorespiratory fitness (Figure 2.).

Discussion

In the present study, we found inverse associations of the measures of cardiorespiratory fitness with aortic stiffness among children and adolescents with chronic disease or physical disabilities. However, the relationships between cardiorespiratory fitness and aortic stiffness were partly explained by waist circumference. We also found that a higher waist circumference had strong and consistent relationship to a higher aortic stiffness. Furthermore, higher waist circumference and BMI-SDS were associated with a lower peripheral arterial tone as indicated by a lower AIX%. Finally, we observed no relationship between sports participation and arterial stiffness.

To the best of our knowledge, this is the first study on the associations of directly assessed $\dot{V}O_{2peak}$ with arterial stiffness among children and adolescents with chronic diseases or physical disabilities. In conjunction with some other studies, we found that better cardiorespiratory fitness was linked to lower aortic stiffness[5,6]. However, the associations of $\dot{V}O_{2peak}$ per body weight and $\dot{V}O_{2peak}$ per FFM with arterial stiffness were partly explained by waist circumference. Similarly, one study found that an inverse association between cardiorespiratory fitness and arterial stiffness was explained by body adiposity among children aged 10 years[32]. These results are in line with the observations that the associations between $\dot{V}O_{2peak}$ relative to body weight and cardiometabolic risk factors are confounded by body adiposity[33,34].

In our previous study, maximal work load by FFM as a measure of cardiorespiratory fitness, was inversely associated with arterial stiffness in children aged 6–8-years independent of body fat percentage[35]. We found that $\dot{V}O_{2peak}$ relative to FFM was attenuated after further adjustment for waist circumference, but remained at borderline significance. Furthermore, controlling for BMI-SDS or body fat percentage had no effect on the relationship between VO_{2peak} relative to FFM and arterial stiffness. These results together indicate that better cardiorespiratory fitness is related to more compliant arteries and that this relationship is not completely due to lower levels of body adiposity in subjects with higher cardiorespiratory fitness. However, more research on the associations of cardiorespiratory fitness with arterial fitness with an appropriate scaling of $\dot{V}O_{2peak}$ are warranted to further clarify the independent role of higher cardiorespiratory fitness of reduced arterial stiffness in children and adolescents. Nevertheless, our results suggest in addition to weight management, improvements in cardiorespiratory fitness may improve arterial stiffness in children and adolescents with chronic diseases or physical disabilities.

Previous studies have suggested a threshold of 35–46 mL/kg/min for $\dot{V}O_{2peak}$ to identify apparently healthy children with increased cardiometabolic risk[36]. We found that a $\dot{V}O_{2peak}$ per body weight lower than 35 mL/kg/min was the optimal threshold for identifying those with increased PWVao and the threshold for identifying children and adolescents with increased AIX% was 51 mL/FFM/min. These slight differences in the cutoffs are probably due to the differences in the outcome measures, methods used to assess cardiorespiratory fitness and to measure or estimate

$\dot{V}O_{2peak}$ as well as the populations studied. We also analyzed boys and girls together to achieve a better statistical power whereas other studies have provided separate cutoffs for boys and girls. However, our results along with the results from previous studies suggest that $\dot{V}O_{2peak}$ below 35–40 mL/kg/min is related to increased cardiometabolic risk in children and adolescents.

Obesity has been consistently linked to increased arterial stiffness in children and adolescents[8]. Similarly, we found that particularly waist circumference was directly associated with arterial stiffness in children and adolescents with chronic diseases and physical disabilities independent of cardiorespiratory fitness. However, we found relatively weak associations of BMI-SDS and body fat percentage with arterial stiffness. An explanation for these inconsistent findings may be that abdominal adiposity has a pronounced negative impact on arterial health in children and adolescents[37]. Furthermore, we found that higher levels of body adiposity were related to lower arterial tone at rest. We[35] and others[38] have previously observed inverse associations between body adiposity and peripheral arterial tone in children and adolescents. One reason for these observations may be that overweight may increase arterial diameter and thereby compensate the negative effects of body adiposity on arterial stiffness[38].

We observed that waist circumference exceeding 73 cm and waist circumference-SDS above -0.05 units were the optimal cut-offs for identifying children and adolescents with increased arterial stiffness. These cut-offs corresponding to an average waist circumference in the Dutch population, suggest that waist circumference already at normal range at the population level is associated with increased arterial stiffness in children and adolescents with chronic diseases or physical disabilities. These findings are supported by the study showing an increased cardiovascular mortality over a 40 year follow-up already among those who had a BMI at the mid-normal range during adolescence[39].

Previous studies have found either inverse or no association between habitual physical activity and the measures of arterial stiffness in children and adolescents[13,40,41]. We observed no differences in arterial stiffness between sports participants and non-sports participants. One reason for our observations may be that sports participation among children and adolescents with chronic diseases or physical disabilities is insufficient in frequency, duration, or intensity to elicit favorable effects on arterial stiffness. Accordingly, there is some evidence that despite the high prevalence of sports participation, the majority of children and adolescents with chronic diseases and physical disabilities fail to meet the physical activity recommendations[42]. Another explanation may be that there may not be a large difference in total habitual physical activity among sports participants and non-participants[23].

The strengths of the present study include valid and reproducible methods used to assess cardiorespiratory fitness, body composition, and arterial stiffness in a relatively large sample of children and adolescents with chronic diseases or physical disabilities. This study had few limitations. We were not able to assess pubertal status of the participants, nor were dietary factors recorded. We also used sports participation as a proxy for physical activity instead of objectively measured physical activity. We defined chronic disease using a non-categorical approach that considers chronically-ill young people as one population rather than specific disease classes[43]. The current sample size prohibited a sub-group analysis in specifying the disease classes. Furthermore, we analyzed boys and girls combined because of the limited statistical power to analyze boys and girls separately. We found no evidence on the effect modification of sex, but the results of some previous studies suggest that the association between cardiorespiratory fitness and arterial health is stronger in boys than in girls[7]. Furthermore, longitudinal studies are needed to study whether the effects of arterial stiffness during childhood and adolescence on cardiovascular diseases in adulthood are different in boys and girls.

In conclusion, lower cardiorespiratory fitness and a higher waist circumference were associated with a higher arterial stiffness in children and adolescents with chronic diseases or physical disabilities in the present study. However, the associations of cardiorespiratory fitness were partly explained by waist circumference. Furthermore, we found no association between sports participation and arterial stiffness. We also found that thresholds of <35 mL/kg/min for VO_{2peak}, >73cm for waist circumference, and >-0.05 units for waist circumference-SDS were associated with increased arterial stiffness. Taken together, these results suggest that interventions aiming to decrease body adiposity and to improve cardiorespiratory fitness may improve arterial stiffness children and adolescents with chronic diseases or physical disabilities. However, intervention studies are warranted to confirm the findings of the present study.

Declaration of Conflicting Interests

The Authors declares that there is no conflict of interest

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Author contribution

EAH, KL, AVM, OV, JG, FJGB, HW, MZ, and TT contributed to conception or design of the study and analysis or interpretation of the data of the present study. EAH and KL drafted the manuscript and AVM, OV, JG, FJGB, HW, MZ, and TT critically revised the manuscript. All authors gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

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Figure legends

Figure 1. ROC curves of the efficacy of the measures of cardiorespiratory fitness and body adiposity to identify children and adolescents with chronic diseases or physical disabilities with increased aortic pulse wave velocity (≥ 1 standard deviation from reference values[28]. AUC indicates the area under the curve (95% confidence interval, CI).

Figure 2. ROC curve of the efficacy of cardiorespiratory fitness to identify children and adolescents with chronic diseases or physical disabilities with increased peripheral arterial tone (augmentation index (AIX%) ≥ 1 standard deviation from reference values[29]. AUC indicates the area under the curve (95% confidence interval, CI). FFM = fat free mass.