


Physical activity modulates arterial stiffness in children with congenital heart disease: A CHAMPS cohort study*

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Funding information

Jim Pattison Children's Hospital Foundation (Saskatoon, Saskatchewan, Canada), Grant/Award Number: #416803, Natasha Boyes Canadian Institutes of Health Research (CIHR PGS), Dr. Corey R. Tomczak Heart and Stroke Foundation of Canada

Abstract

Children with congenital heart disease are at risk for developing increased arterial stiffness and this may be modulated by physical activity.

Objective: To compare arterial stiffness in high- and low-physically active children with congenital heart disease and healthy age- and sex-matched controls.

Patients: Seventeen children with congenital heart disease (12 ± 2 years; females = 9), grouped by low- and high-physical activity levels from accelerometry step count values, and 20 matched controls (11 ± 3 years; females = 9) were studied.

Outcome Measures: Carotid-radial pulse wave velocity was assessed with applanation tonometry to determine arterial stiffness. Body composition and 6-min walk test measures were performed. Data were analyzed using analysis of variance and multiple regression. Significance was $P < .05$.

Results: Arterial stiffness was increased in low-physically active children with congenital heart disease (9.79 ± 0.97 m/s) compared to high-physically active children with congenital heart disease (7.88 ± 0.71 m/s; $P = .002$) and healthy-matched controls (8.67 ± 1.28 m/s; $P = .015$). There were no differences in body composition measures between groups (all $P > .05$), but 6-min walk test distance was less in both congenital heart disease groups (high-physically active: 514 ± 40 m; low-physically active: 539 ± 49 m) versus controls (605 ± 79 m; all $P < .05$). Average daily step count significantly predicted arterial stiffness in children with congenital heart disease ($R^2 = 0.358$) with a negative correlation ($R = -0.599$, $P = .011$), while % fat mass ($P = .519$) and % lean mass ($P = .290$) did not predict arterial stiffness.

Conclusions: Low-physically active children with congenital heart disease have increased arterial stiffness compared to high-physically active children with congenital heart disease and healthy-matched controls. Regular physical activity in children with congenital heart disease may modulate arterial stiffness.

KEYWORDS

accelerometry, body composition, functional capacity, pulse wave velocity

*CHAMPS: Children's Healthy-Heart Activity Monitoring Program in Saskatchewan

1 | INTRODUCTION

Children with congenital heart disease (CHD) are often less physically active^{1–3} and have lower functional capacity than their healthy counterparts,⁴ which may predispose children with CHD to be more prone to increased arterial stiffness.⁵ Arterial stiffness has been found to negatively correlate with fitness and daily physical activity in healthy children.⁶ However, the relationship between fitness and arterial stiffness in healthy children is diminished when body composition measurements are considered,⁶ suggesting that anthropometric determinants of arterial stiffness may play a larger role than physical activity in modulating arterial stiffness. Conversely, other evidence demonstrates that overweight and obesity rates are comparable between children with CHD and healthy children,⁷ suggesting that the increased arterial stiffness reported in children with CHD⁵ is less so attributable to body composition and rather may be modulated by physical activity. Studies to date have not identified whether arterial stiffness is differentially affected by physical activity levels in children with CHD. Knowing this relationship is critical as we investigate clinically important modifiable risk factors to reduce arterial stiffness and cardiovascular disease risk, particularly as physical activity is known to influence arterial stiffness in healthy adults⁸ and children.⁹ Therefore, we tested the hypothesis that low-physically active children with CHD would have increased arterial stiffness compared to high-physically active children with CHD and healthy-matched controls. We also quantified the relationship between arterial stiffness and physical activity in children with CHD and healthy-matched controls.

2 | METHODS

Twenty-one children with CHD and 23 age- and sex-matched healthy children were tested. Parental consent and child assent were obtained prior to all study activities. Pretest instructions included avoiding testing-day exercise and caffeine consumption, avoiding large meals within 2 hours of testing, and maintaining normal medication use. Ethical approval for this study was obtained from the University of Saskatchewan Research Ethics Board, Biomedical Panel.

Participants rested supine for 10-min before recording sequential ECG-gated (Bio Amp, ADInstruments Bella Vista, New South Wales, Australia) measurements of pulse wave velocity using applanation tonometry (Mikro-tip Catheter Transducers model SPT-301, Millar Instruments, Inc, Houston, Texas) at the carotid and radial sites.^{9,10} Distance between the sternal notch and the carotid and radial sites were each measured on the surface of the body.¹¹ Using the foot-to-foot method,¹¹ pulse wave velocity was calculated as $D \times \Delta t^{-1}$ where D was the distance (m) between carotid and radial sites and Δt was the time (s) difference between carotid and radial pulse waves.¹¹ Pulse wave velocity was calculated as the average of 10 consecutive beats to represent a full respiratory cycle.¹¹ Applanation tonometry and ECG signals were recorded and integrated through a data acquisition hardware system at 1 kHz/s (Powerlab 16/30, ADInstruments) and analyzed offline (LabChart 7.0, ADInstruments).

Dual-energy x-ray absorptiometry (DXA) was used to assess body composition. A total body DXA scan was taken in array mode by a certified technologist (QDR Discovery Wi; Hologic, Inc, Bedford, Maryland) and analyzed using QDR software for Windows XP (QDR Discovery, Hologic, Inc). Areal variables included total lean mass (g) and total fat mass (g), which were used to calculate total % lean mass and total % fat mass for statistical analysis.

Participants performed a 6-min walk test (6MWT) to determine functional capacity using American Thoracic Society guidelines.¹² Participants then wore a triaxial accelerometer (GT3XPB, ActiGraph Corp, Pensacola, Florida) for 7 consecutive days to assess physical activity levels. Physical activity data were processed offline using the Freedson 2005 cut points for children¹³ to yield average daily step count values.

By employing a median split approach using daily step count values comparable to prior work,¹⁴ children with CHD were categorized as high-physically active (≥ 8987 steps/day = high-physically active) or low-physically active (< 8987 steps/day = low-physically active). The median split yielded a cut off (~ 9000 steps/day) comparable to previously documented averages in children aged 11–13 years¹⁵ and adolescents.¹⁶ Further, the average step count in our high-physically active group was comparable to the control group. Group differences in outcome variables were determined using analysis of variance with Student-Newman-Keuls post hoc when F -values were significant. A chi-square analysis assessed the difference in sex distribution between groups. Stepwise multiple regression was used to assess the relationships of physical activity (step count) and body composition (% fat and lean mass) with pulse wave velocity in children with CHD and in controls. Significance was accepted at $P < .05$ (IBM SPSS version 24.0, Chicago, Illinois).

3 | RESULTS

Data from two children with CHD were excluded from analysis due to one child having paced cardiac cycles during assessment and the other having low-quality pulse wave velocity data. Five additional participants (two CHD, three controls) did not have complete accelerometry data (devices were lost or not returned). Therefore, 17 children with CHD and 20 healthy controls were included in the final analysis. Table 1 provides diagnostic information for individual children with CHD.

Table 2 shows descriptive and outcome data for the high-physically active CHD group, the low-physically active CHD group, and controls. There were no differences in body composition measurements between groups. High-physically active CHD and low-physically active CHD had lower functional capacity than controls, as assessed via 6MWT (both $P < .05$). By design, average daily step count was significantly lower in low-physically active CHD compared to high-physically active CHD and controls (both $P < .05$). Notably, there was no difference in average daily step count between high-physically active CHD and controls indicating similar physical activity levels between these two groups ($P = .261$).

TABLE 1 Diagnostic features of children with CHD

CHD patient #	Diagnosis	Surgical procedure	Medications
1	Transposition of great arteries	Arterial switch procedure, branch pulmonary artery stenosis repair	-
2	Hypoplastic left heart syndrome	Fontan procedure	Aspirin, enalapril
3	Ebstein's anomaly	Tricuspid valve repair, bidirectional cavopulmonary shunt	-
4	Tetralogy of Fallot	Full repair	-
5	Double inlet left ventricle	Fontan procedure	Aspirin
6	Hypoplastic left heart syndrome	Fontan procedure	-
7	Tricuspid atresia	Fontan procedure	Aspirin
8	Coarctation of the aorta	Full repair, balloon angioplasty recurrent coarctation	-
9	Pulmonary stenosis, tricuspid regurgitation, atrial septal defect	Balloon pulmonary valvuloplasty, tricuspid valve repair and atrial septal defect closure	-
10	Congenital corrected transposition of great arteries	Unrepaired	-
11	Ventricular septal defect	Full repair	-
12	Tetralogy of Fallot	Full repair	-
13	Tetralogy of Fallot	Full repair	Thyroxine
14	Coarctation of aorta, ventricular septal defect	Full repair	-
15	Tetralogy of Fallot	Full repair	-
16	Tetralogy of Fallot	Full repair	-
17	Left atrial isomerism, double outlet right ventricle, pulmonary stenosis	Full repair	-

CHD patient diagnosis, surgical procedure details (if performed), and medications. Abbreviation: CHD, congenital heart disease.

Low-physically active CHD had greater arterial stiffness compared to high-physically active CHD and controls ($P = .005$; Figure 1). There was no difference in arterial stiffness between high-physically active CHD and controls ($P = .112$). Average daily step count significantly predicted arterial stiffness in children with CHD ($R^2 = 0.358$) with a negative correlation ($R = -0.599$, $P = .011$; Figure 2), while % fat mass ($P = .519$) and % lean mass ($P = .290$) did not predict arterial stiffness in children with CHD. In contrast, average daily step count did not significantly predict arterial stiffness in controls ($P = .339$; Figure 2).

4 | DISCUSSION

The major novel finding of this study was that low-physically active children with CHD had increased arterial stiffness compared with high-physically active children with CHD and healthy-matched controls. Arterial stiffness was negatively related to physical activity but not body composition measures in children with CHD. Lastly, functional capacity was significantly lower in both low- and high-physically active children with CHD compared to healthy-matched controls and there were no differences in body composition measures between groups.

Together, our findings suggest that physical activity may be key in modulating the vascular health of children with CHD, without a differential benefit to functional capacity in either high- or low-physically active children with CHD and with similar body composition measures between CHD groups and controls.

Prior work has shown that physical activity levels may be fundamental in the progression of arterial stiffness, as even in the absence of CHD, both children⁹ and adults¹⁷ have increased arterial stiffness when more sedentary. Consistent with our findings of a negative relationship between physical activity and arterial stiffness in children with CHD, others have reported in healthy prepubescent children that arterial stiffness was negatively correlated with cardiorespiratory fitness and step count.⁶ This observation has also been replicated in adults without chronic disease.⁸ One prior study in preschool-aged children with CHD revealed no indication of increased arterial stiffness,¹⁸ whereas similarly aged school-age children with CHD as in our study have been shown to have increased arterial stiffness compared to healthy controls.⁵ Therefore, children with CHD are more prone to increased arterial stiffness, but the role of physical activity on arterial stiffness has not been previously investigated. We extend prior reports by demonstrating that physical activity volume may help modulate

TABLE 2 Participant demographics, body composition, functional capacity, and physical activity levels

	High-physically active CHD	Low-physically active CHD	Controls	ANOVA P value
Total n (male:female)	9 (5:4)	8 (3:5)	20 (11:9)	.675
Age, yrs	11 ± 2	12 ± 3	11 ± 3	.640
Height, cm	140 ± 11	146 ± 15	148 ± 18	.471
Weight, kg	37 ± 12	40 ± 13	41 ± 15	.819
BMI, kg/m ²	18.7 ± 4.0	18.3 ± 3.6	18.0 ± 2.9	.875
Waist circumference, cm	66 ± 11	66 ± 10	65 ± 9	.949
Fat mass, %	24 ± 8	23 ± 5	20 ± 5	.314
Lean mass, %	75 ± 11	73 ± 5	76 ± 5	.601
6MWT distance, m	514 ± 39*	539 ± 49*	605 ± 79	.003
Step count, steps/day	11679 ± 2312	5562 ± 2293*†	10075 ± 3780	.001

Values are means ± SD. Participant demographics, body composition, functional capacity, and daily physical activity levels by CHD (high- and low-physically active groups) and control groups.

Abbreviations: 6MWT, 6-min walk test; BMI, body mass index; CHD, congenital heart disease.

*Significantly different versus controls, $P < .05$.

†Significantly different versus high-physically active CHD, $P < .05$.

arterial stiffness in children with CHD, as our low-physically active CHD group had significantly greater arterial stiffness compared to our high-physically active CHD group and healthy-matched controls. Moreover, there was no significant difference in arterial stiffness between high-physically active CHD and healthy-matched controls, further suggesting that regular physical activity may mitigate increased arterial stiffness in children with CHD.

Low physical activity increases overweight and obesity risk,¹⁹ and these factors adversely contribute to arterial stiffness in children.²⁰ Sakuragi et al⁶ found that BMI, waist circumference, and % body fat were all independently and positively associated with arterial stiffness in healthy children, and more so than exercise capacity. Similarly, Pandit et al²¹ assessed 250 children (71% overweight or obese) and reported waist circumference, BMI, body fat and physical activity to all be independently associated with arterial stiffness. Despite lower levels of physical activity in children with CHD,¹⁻³ overweight and obesity rates may often be comparable to the general population.⁷ In this study, children with CHD were not found to be overweight or obese and were similar across several clinically relevant body composition measurements (eg, BMI, waist circumference) compared to healthy-matched controls. Moreover, neither % body fat nor % lean mass was correlated with pulse wave velocity in our children with CHD. Therefore, our findings of greater arterial stiffness in low-physically active children with CHD may be more causally attributed to physical activity levels, rather than established anthropometric determinants of arterial stiffness.

Children with CHD typically participate in less regular physical activity than their healthy counterparts,¹⁻³ and this may contribute to a reduction in functional capacity.⁴ In the current investigation, however, both high-physically active CHD and low-physically active CHD groups had similar functional capacity measured by 6MWT distance, and both CHD groups had lower functional capacity than healthy-matched

control participants. Our novel finding of similarly lower functional capacity despite differences in daily physical activity suggests that factors related to CHD^{22,23} likely contribute to the observed lower functional capacity in our CHD study groups.

5 | LIMITATIONS

Our study has a few important considerations. First, it is possible that the low-physically active CHD group is limited by their congenital heart condition; that is, the more serious nature of the CHD in these children may have an independent effect on arterial stiffness. In defense, the distribution of simple and complex lesion types between groups was nearly identical, with the majority of participants in both groups having

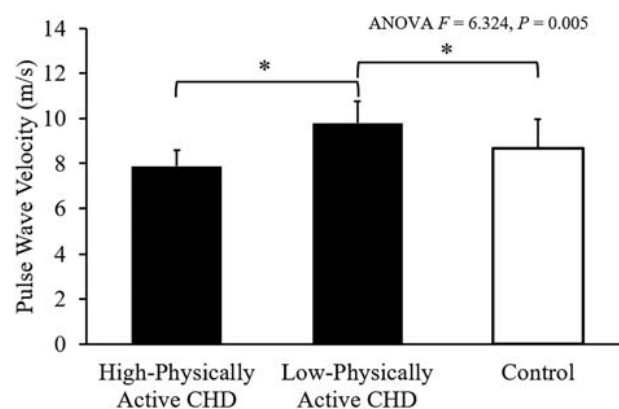


FIGURE 1 Arterial stiffness (measured by carotid-radial pulse wave velocity) in high- and low-physically active (measured by average daily step count) children with congenital heart disease (CHD) and healthy age- and sex-matched children. *Significantly different between groups ($P < .05$)

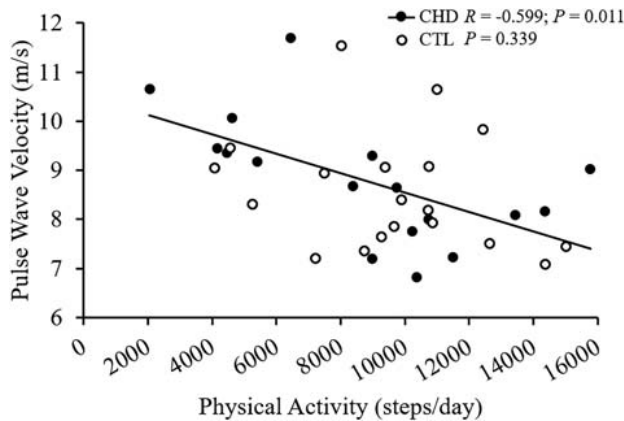


FIGURE 2 Relationship between physical activity (measured by average daily step count) and arterial stiffness (measured by carotid radial pulse wave velocity) in children with congenital heart disease (CHD) and healthy age- and sex-matched children

complex lesions. Further, the small sample size in this study precluded the analysis of CHD type on arterial stiffness and physical activity levels. Second, our smaller sample of children with CHD has similar body composition to our control group, therefore, the variance in body composition types is not represented in our study. Thus, we cannot preclude the possibility that body composition does affect arterial stiffness. However, in our current cohort, both groups were similar in body composition and body composition did not correlate with arterial stiffness. This discrepancy with previous literature may be due to volunteer bias, whereby healthier, more active families were more likely to volunteer for a physical activity related study.

6 | CLINICAL RELEVANCE

Elevated arterial stiffness is associated with increased risk of future cardiovascular disease^{24,25} and mortality²⁵ in older adults, even when individuals are seemingly otherwise healthy.²⁵ Chronic physical inactivity in youth increases the risk of becoming a sedentary adult and developing latent chronic disease,¹ including stiffer arteries,⁹ which can be countered by regular exercise and increasing cardiorespiratory fitness.^{6,26} It is reasonable to predict that elevated arterial stiffness in children may have similar health-related outcomes,²⁰ however, there is no prospective study that establishes this link. Given this knowledge gap, long-term prospective data assessing the link between arterial stiffness and cardiovascular disease outcomes in children with CHD is warranted. Our findings highlight the importance of physical activity promotion for children with CHD for mitigating arterial stiffness.

7 | CONCLUSION

Physical activity modulates arterial stiffness, and when children with CHD and controls of similar physical activity levels are compared, there is no difference in arterial stiffness. Low-physically active children with CHD have increased arterial stiffness when compared to high-physically active CHD and healthy controls, despite having a similar

functional capacity as high-physically active CHD. Therefore, physical activity may modulate arterial stiffness, but not functional capacity, in children with CHD. This finding is independent of anthropometric determinants that are known to adversely increase arterial stiffness in children with CHD, as there were no differences in body composition parameters between our study groups and body composition was not related to pulse wave velocity in our children with CHD.

ACKNOWLEDGMENTS

We gratefully acknowledge the participants and families of CHAMPS (Children's Healthy-Heart Activity Monitoring Program in Saskatchewan), and CHAMPS collaborators Dr. Lauren Sherar, Lynne Telfer, RN, Juanita Praksis, RN, Marie Penner, RN, and Angela Wiens, RN.

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Participant recruitment and data collection: Boyes, Fusnik, Hogeweide, Fries, Runalls, Kakadekar, Pharis, Pockett, Bradley, Wright, Erlandson, Tomczak

Data processing: Boyes, Stickland, Fusnik, Hogeweide, Fries, Haykowsky, Barill, Bradley, Erlandson, Tomczak

Statistical analyses: Boyes, Stickland, Fusnik, Hogeweide, Fries, Haykowsky, Barill, Bradley, Erlandson, Tomczak

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Manuscript drafting: Boyes, Bradley, Erlandson, Tomczak

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CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose.

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How to cite this article: Boyes NG, Stickland MK, Fusnik S, et al. Physical activity modulates arterial stiffness in children with congenital heart disease: A CHAMPS cohort study. *Congenital Heart Disease*. 2018;13:578–583. <https://doi.org/10.1111/chd.12614>