Associations between arterial stiffness and cardiovascular disease risk factors among black South African children

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Background. A limited number of studies have researched the associations between conventional cardiovascular disease (CVD) risk factors and arterial stiffness in children.

Objectives. To explore the associations between specific conventional CVD risk factors and arterial stiffness in black South African (SA) children.

Methods. This cross-sectional study included 59 children (male:17; female:42). The mean age (and associated standard deviation) of the participants was 11.15 (1.40) years. Conventional CVD risk factors included body mass index (BMI), waist circumference (WC), hip circumference, systolic blood pressure (SBP), resting heart rate (RHR), peak oxygen consumption (VO$_2$peak) and physical activity. Pearson's correlation was used to measure associations between arterial stiffness, expressed as the stiffness index (SI), and CVD risk factors. Hierarchical multiple regression analysis adjusting for age was performed to identify associations between the independent variables (VO$_2$peak, SBP, BMI, physical activity, RHR and WC) and the dependent variable (SI).

Results. Arterial stiffness was found to be significantly positively correlated with age (r=0.52; p=0.03) and significantly negatively correlated with VO$_2$peak (r=−0.53; p=0.03) in male participants. Following regression analysis, the association with age (r^2=0.27; p=0.03) and SI remained significantly independent. When means were combined across the two gender groups, age (r=0.27; p=0.04) and RHR (r=0.26; p=0.05) were found to be significantly positively correlated with SI. Following regression analysis, both age (r^2=0.07; p=0.04) and RHR (r^2=0.15; p=0.02) remained significantly independently associated with SI.

Conclusion. Age and RHR appear to be strong predictors of arterial stiffness in black SA children.

Cardiovascular disease (CVD) is the leading cause of mortality and morbidity worldwide and is estimated to cause 17.3 million deaths per year.[1] CVD incidence is strongly associated with a set of conventional risk factors, which include increased waist circumference (WC), high body mass index (BMI), high systolic blood pressure (SBP), increased levels of low-density lipoprotein, high blood glucose levels, low levels of physical activity and poor cardiorespiratory fitness.[2]

However, screening for these conventional risk factors may underestimate the risk of CVD, especially in asymptomatic children.[3] Therefore, other non-conventional risk factors may be important to consider. Pulse wave velocity can be used as an indicator of arterial stiffness, which suggests structural changes in arterial walls that precede the events of atherosclerosis and CVD.[4] Arterial stiffness has been reported to be a notable risk factor for developing future CVD independent of conventional risk factors in adults.[4] Similarly, arterial stiffness has been shown to be positively associated with several conventional risk factors for CVD in children,[5] although findings in paediatric studies are inconsistent.

Reed *et al.*[6] determined the predictors of arterial stiffness in a sample of 99 Canadian children (aged 9 - 11 years). The results showed that children in the highest fitness quartile had 34% greater arterial compliance than children in the lower quartiles. Other predictors of arterial stiffness included body mass, SBP and maturation,[6] in accordance with a US population-based study that found significant associations between arterial stiffness, age, gender, BMI and SBP among 343 healthy adolescents and young adults (aged 15 - 28 years).[7] Conflicting results were reported in a European study, which found no significant correlations between arterial stiffness, gender, age, BMI, Tanner stage or SBP levels among 38 non-obese adolescents (mean age and associated standard deviation (SD): 15.02 (1.94) years).[8] The same study reported a significant association between arterial stiffness and SBP among 68 obese adolescents (mean (SD) age: 13.27 (2.31) years).[8] This could imply that early vascular damage is more apparent in obese adolescents than in their lean counterparts.

A greater understanding of arterial stiffness and its association with conventional CVD risk factors is warranted. Furthermore, it has been reported that black South African (SA) children are at an increased risk of developing CVD.[9] Similarly, increased arterial stiffness has been reported in black SA boys (aged 6 - 8 years) compared with their white counterparts.[10] Thus, this study aimed to explore associations between specific conventional CVD risk factors and arterial stiffness in black SA children.

Methods

Participants

This cross-sectional study recruited 59 black SA children (17 male, 42 female) from an urban primary school in the province of KwaZulu-Natal, SA, in June 2015. The mean (SD) age of participants was 11.15 (1.40) years. The inclusion criteria specified that black children between the ages of 10 and 13 years and who

were healthy, without any known medical conditions, were eligible for participation in the study.

Measurements

Measurements were taken on five consecutive days between 09:00 and 12:00 in a quiet room at the school. Conventional CVD risk factor measurements included BMI, WC, hip circumference, SBP, resting heart rate (RHR) and peak oxygen consumption (VO$_2$peak). Participation in physical activity was also included as an associated factor and was measured according to a modified version of the self-administered physical activity questionnaire for older children (PAQ-C).[11] The questionnaire measures general physical activity levels in children aged 8 - 14 years during a typical week in a school year. The questionnaire includes nine questions based on a broad spectrum of activities taking place during physical education, first and second breaks, days and evenings, and over the weekend. Question 1 was adapted somewhat in that some sport activities (cross-country skiing, ice hockey and badminton) included in the original questionnaire were replaced with sport activities more suitable to the SA context (cricket, athletics and rugby). All nine questions were scored on a 5-point Likert scale assessing frequency and intensity of activities. Participants were categorised as having low, moderate or high physical activity based on their final mean score. A score of 1.00 - 2.33 indicated low physical activity, a score of 2.34 - 3.66 was taken as a moderate physical activity level, and a high level of physical activity was taken as a score between 3.67 and 5.00.[11]

WC was measured midway between the lowest rib and the iliac crest in a standing position using a measuring tape.[12] A digital scale (OMRON Healthcare, SA) was used to measure body weight, recorded to the nearest 0.1 kg. A portable stadiometer (Alturaexata, Brazil) was used to measure height, recorded to the nearest 0.1 cm. BMI was calculated as body weight divided by height squared (kg/m^2), and BMI z-scores were based on the Centers for Disease Control and Prevention standards.[13] SBP and RHR were measured three times in a seated position using a digital automated blood pressure device (Connex ProBPTM 3400., USA) after 5 minutes of resting. The average of the second and third readings was analysed for both SBP and RHR. SBP z-scores were subsequently calculated according to the National Heart, Lung and Blood Institute standards.[14] VO$_2$peak was estimated using the 20-metre shuttle run test.[15] Léger and Lambert's[16] equation (VO$_2$peak = 31.025 + (3.238 × velocity) – (3.248 × age) + (0.1536 × age × velocity)) was used to obtain indirect VO$_2$peak values. The arterial stiffness index (SI), an indicator of large artery stiffness, was derived from digital volume pulse using the PulseTrace PCA2 photoplethysmographic device (Micro Medical,

UK). This device has also been used in other paediatric studies and has been validated by comparing results with carotid-femoral pulse wave velocity, the gold standard for measuring arterial stiffness.[17,18] The average of two SI measurements was calculated and expressed in metres per second. Participants were tested while lying supine.

Statistical analysis

Statistical analyses were performed using SPSS for Windows (version 20.0, IBM Corp., USA). Normally distributed data were expressed as means and SDs. The Kolmogorov-Smirnov test was used to test the assumption of Gaussian distribution. Pearson's correlation was used to measure associations between SI and CVD risk factors. Hierarchical multiple regression analysis adjusting for age was conducted to identify associations between the independent variables (VO$_2$peak, SBP, BMI, physical activity, RHR and WC) and the dependent variable (SI). The independent variables were separated into two blocks: age in one block, and VO$_2$peak, SBP, BMI, physical activity, RHR and WC in the other. Variance of inflation factors was calculated to investigate collinearity in any of the analyses. A significance level of $p \leq 0.05$ was used.

Ethical considerations

Ethical clearance was obtained from the University of Zululand Research Ethics Committee (ref. no. UZREC171110-030). All participants and parents gave their informed consent before commencement of the study. In addition, permission to conduct the study was also obtained from the KwaZulu-Natal Department of Education (ref. no. 2/4/8/815). The study was conducted in accordance with the World Medical Association Declaration of Helsinki on ethical principles involving the use of human subjects in medical research.[19]

Results

Of the 59 participants, 17 were male (29%) and 42 female (71%). Regression coefficients (Table 1) showed that a large proportion of the variation in SI among male participants was explained by age (β=0.52; p=0.03) and VO$_2$peak (β=−0.41; p=0.39). In female participants, VO$_2$peak (β=−0.38; p=0.21) and RHR (β=0.26; p=0.18) explained the largest proportion of the variation in SI. When results were combined across the gender groups (Table 2), the largest proportion of the variation in SI was explained by age (β=0.26; p=0.04), RHR (β=0.24; p=0.09) and VO$_2$peak (β=0.24; p=0.32).

Among male participants, SI was found to be significantly positively correlated with age (r=0.52; p=0.03) and significantly negatively correlated with VO$_2$peak (r=−0.53; p=0.03). Following regression analysis, the association between age (r^2=0.27; p=0.03) and SI

Table 1. Baseline characteristics of male and female study participants

	Male (n=17)		Female (n=42)	
Variable	Mean (SD)	β (p-value)	Mean (SD)	β (p-value)
SI (ms^{-1})	5.40 (0.62)	NA	5.53 (0.58)	NA
Age (years)	10.82 (1.28)	0.52 (0.03)	11.28 (1.43)	0.15 (0.31)
BMI z-score	1.13 (1.39)	0.18 (0.61)	0.72 (1.17)	0.10 (0.69)
RHR (bpm)	79.11 (6.99)	−0.06 (0.88)	80.66 (7.54)	0.26 (0.18)
Physical activity	2.46 (0.29)	−0.28 (0.34)	2.58 (0.56)	0.02 (0.87)
WC (cm)	41.85 (24.51)	−0.15 (0.70)	55.98 (18.16)	−0.04 (0.84)
SBP (z-score)	1.51 (1.02)	0.25 (0.51)	0.84 (0.78)	−0.17 (0.31)
VO$_2$peak (mL.kg^{-1}min^{-1})	41.44 (2.11)	−0.41 (0.39)	40.73 (4.00)	−0.38 (0.21)

SD = standard deviation; SI = stiffness index; NA = not applicable; BMI = body mass index; RHR = resting heart rate; bpm = beats per minute; WC = waist circumference; SBP = systolic blood pressure; VO$_2$peak = peak oxygen consumption

Table 2. Baseline characteristics of study participants combined across gender groups (*N*=59)

Variable	Mean (SD)	*β* (*p*-value)
SI (ms⁻¹)	5.5 (0.59)	N/A
Age (years)	11.15 (1.4)	0.26 (0.04)
BMI *z*-score	0.78 (1.42)	0.09 (0.58)
RHR (bpm)	80 (7.37)	0.24 (0.09)
Physical activity	2.51 (0.41)	−0.03 (0.79)
WC (cm)	51.91 (20.10)	−0.02 (0.88)
SBP (*z*-score)	1.05 (0.89)	−0.14 (0.29)
VO$_2$peak (mL.kg⁻¹ min⁻¹)	40.93 (3.55)	0.24 (0.32)

SI = stiffness index; BMI = body mass index; RHR = resting heart rate; bpm = beats per minute; WC = waist circumference; SBP = systolic blood pressure; VO$_2$peak = peak oxygen consumption.

remained significantly independent. No significant correlations were found for any of the variables with SI among female participants. When means were combined across the gender groups (Table 2), age (r=0.27; p=0.04) and RHR (r=0.26; p=0.05) demonstrated significant positive correlations with SI. Following regression analysis, the association with SI remained significantly independent for both age (r^2=0.07; p=0.04) and RHR (r^2=0.15; p=0.02).

Discussion

This study is the first to report on the associations between conventional CVD risk factors and arterial stiffness in black South African children. The primary findings indicate that arterial stiffness was independently associated with age in male participants, whereas none of the assessed variables showed a correlation with arterial stiffness in female participants. When results were combined across the two gender groups, SI, as an indication of arterial stiffness, was found to be independently associated with both age and RHR.

Studies from Brazil and Canada have reported associations between conventional CVD risk factors and arterial stiffness in children,[5,20] although the cross-sectional study of 485 Canadian children (aged 12 - 14 years) found no significant associations between arterial stiffness, conventional CVD risk factors and physical activity levels.[20] The authors concluded that associations between arterial stiffness and physical activity may appear in children only when activity levels are at either end of the physical activity continuum.[20] This is in line with findings from our study, in which participants' physical activity levels were observed as moderate (mean (SD) 2.51 (0.41)) and without significant association with SI.

The mentioned study among 231 Brazilian children (aged 9 - 10 years) found significant associations between SI and BMI.[5] This differs from our findings, which showed the only CVD risk factors associated with SI to be RHR and age.

The SI values reported by Walker *et al.*[20] are higher than those found in our study. The mean (and associated SD) values for SI in boys (5.40 (0.62) ms⁻¹) and girls (5.53 (0.58) ms⁻¹) in our study compare favourably with the mean values reported for carotid radial pulse wave velocity in their study (7.63 ms⁻¹ and 7.48 ms⁻¹ for boys and girls, respectively). Combined mean (and associated SD) values for SI found in our study (5.5 (0.59) ms⁻¹) were similar to those reported from the mentioned study among Brazilian children (5.3 (0.52) ms⁻¹).[5] The higher SI values reported by Walker *et al.*[20] could be attributed to the observation that SI increases with age.

Age could be an important variable when studying arterial stiffness, but for a deeper understanding it should be assessed in conjunction with growth and maturation, given that body height at the transition from childhood to adolescence has been reported to affect arterial stiffness.[21]

Associations between RHR and arterial stiffness in children have not been well documented in literature. However, findings on normotensive adults suggest that a higher RHR is independently associated with increased arterial stiffness.[22] In our study, RHR and arterial stiffness appear to be positively associated if the results from the two gender groups are combined, with a dependent association with VO$_2$peak seen among boys. These results suggest that fitness levels may have an important role in the regulation of vascular health in children. Indeed, cardioprotective benefits of VO$_2$peak have been documented and include the capacity for vessel-wall regeneration and angiogenesis.[23]

Study limitations

This study did not consider genetic, metabolic, environmental, socio-economic or maturation-related influences on arterial stiffness. The lack of pubertal staging, mixed ages of the participants and the fairly small sample size may be considered further limitations.

Conclusion

The present study suggests that age and RHR are key predictors of arterial stiffness in black SA children. Furthermore, different gender associations with SI highlight the need for gender-specific CVD risk screening in this population.

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