

Dencker, M., Thorsson, O., Karlsson, M. K., Lindén, C., Wollmer, P., Andersen, L. B. (2012). Aerobic fitness related to cardiovascular risk factors in young children. *European Journal of Pediatrics*, 171, 705-710.

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Aerobic fitness related to cardiovascular risk factors in young children

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Keywords: VO_{2PEAK} , Body fat, DXA, CVD risk factors

Running title: Fitness and CVD risk factors

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Abstract

Low aerobic fitness (VO_{2PEAK}) is predictive for poor health in adults. Cross-sectional study we assessed if VO_{2PEAK} is related to a composite risk factor score for cardiovascular disease (CVD) in 243 children (136 boys and 107 girls) aged 8 to 11 years. VO_{2PEAK} was assessed by indirect calorimetry during a maximal exercise test and scaled by body mass (ml/min/kg). Total fat mass (TBF) and abdominal fat (AFM) were measured by Dual-energy x-ray absorptiometry. Total body fat was expressed as a percentage of total body mass (BF%), and body fat distribution as AFM/TBF. Systolic and diastolic blood pressure (SBP, DBP), and resting heart rate (RHR) were measured. Mean artery pressure (MAP) and pulse pressure (PP) were calculated. Echocardiography, 2-dimensional guided M-mode, was performed and left atrial diameter (LA) was measured and left ventricular mass (LVM) and relative wall thickness (RWT) were calculated. Z-scores (Value for the individual-mean value for group)/SD were calculated, by sex. Sum of z-scores for DBP, SDP, PP, MAP, RHR, LVM, LA, RWT, BF%, AFM, and AFM/TBF were calculated in boys and girls, separately, and used as composite risk factor score for CVD. Pearson correlation revealed significant associations between VO_{2PEAK} and composite risk factor score in both boys ($r=-0.48$ $P<0.05$), and in girls ($r=-0.42$, $P<0.05$). One-way ANOVA analysis indicated significant differences in composite risk factor score between the different quartiles of VO_{2PEAK} ($P<0.001$), thus higher VO_{2PEAK} was associated with lower composite risk factor score for CVD. In conclusion, this sample of young children shows that low VO_{2PEAK} is associated with an elevated composite risk factor score for CVD in both boys and girls.

Introduction

Aerobic fitness, defined as maximum oxygen uptake (VO_{2PEAK}), is an important marker for health and disease. Low aerobic fitness has, in adults, been shown to be a strong predictor for a variety of diseases and all cause mortality [38]. Also, low aerobic fitness in late adolescence has been shown to be associated with other risk factors for cardiovascular disease (CVD) in young adulthood [25, 37]. Aerobic fitness has also been shown to track from childhood into adulthood [1, 37]. It is therefore relevant to investigate health related aspects of VO_{2PEAK} and to provide detailed information of risk accumulation also in young subjects. There have been several reports on the relationships between fitness, by indirect methods, and multiple other risk factors for CVD in representative samples of younger children [3, 4, 7, 19-21, 26]. In contrast, limited data exist on comprehensive relationships between directly measured VO_{2PEAK} and other risk factors for CVD in representative samples of younger subjects [18, 35-36]. No investigation has to our knowledge investigated the relationship between directly measured VO_{2PEAK} and aggregation of physiological risk factors for CVD such as blood pressure and body fat measurements in combination with structural cardiac risk factors for CVD. Thus, the purpose of this study was to investigate the relationships between VO_{2PEAK} and other CVD risk factors in a representative sample of young children, and also estimate the percentage of population that has an elevated risk score as predicted by fitness level.

Materials and Methods

Subjects and anthropometric measures

Recruitment and methodology of the study cohort has been presented previously [9-15]. In brief, 477 children (259 boys and 218 girls) living in homogenous middle class areas in Malmö, Sweden, received an invitation to participate in the study and 248 (140 boys and 108 girls) accepted the invitation. Height and body mass were measured in the laboratory with the child dressed in light clothing. Height was measured to the nearest 1.0 cm and body mass was measured to the nearest kg. Body mass index (BMI) was calculated as body weight in kilograms divided by height in meters squared (kg/m^2). Height and body mass of all invited children were retrieved from the general health data registered by the school nurses, in order to evaluate if a selection bias had occurred. Puberty status was assessed by self-evaluation according to Tanner [17]. The institutional ethics committee of Lund University, Sweden, approved the study. Written informed consent was obtained from the parents of all participating children.

Measurement of Aerobic Fitness

Aerobic fitness was determined by a maximal exercise test performed on an electrically braked cycle ergometer (Rodby rhc, model RE 990, Rodby Innovation AB, Karlskoga, Sweden). All children, regardless of gender, fitness, height and body mass, used the same protocol with an initial workload of 30 Watt (W) and a continuous increase of 15 W per minute. Expired gas was sampled continuously via a mixing chamber and analysed for the concentration of O₂ and CO₂ (Sensor Medics 2900, SensorMedics Inc, Yorba Linda, CA, USA). Measurements were obtained every 20 s during two minutes at rest and during exercise to volitional exhaustion. Heart rate (HR) and respiratory exchange ratio (RER) were recorded throughout the test. Maximum heart rate (max HR) and maximum RER (max RER) were recorded. Maximal oxygen uptake (VO_{2PEAK}) was determined as the highest value during the last minute of exercise and scaled to body mass. The exercise test was considered acceptable if it met one of the following criteria: RER ≥ 1.0, max HR >90% of predicted value (196 beats/min) or signs of intense effort (e.g. hyperpnoea, facial flushing or inability in keeping adequate revolutions/min (53-64)), [5].

Dual-Energy X-Ray Absorptiometry (DXA)

Total body fat mass (TBF) and abdominal fat mass (AFM) were quantified by DXA (DPX-L version 1.3z, Lunar, Madison, WI, USA). Pediatric software was used for children with a weight below 30 kg. Body fat was also calculated as a percentage of total body mass (BF%), and body fat distribution as AFM/TBF. DXA has been shown to provide accurate and precise measurements of body composition [30], including abdominal fat [24].

Blood pressure

A Dinamap paediatric vital signs monitor (model XL, Critikron, Inc, Tampa, FL, USA) was used to measure resting heart rate (RHR), systolic blood pressure (SBP) and diastolic blood pressure (DBP) in the seated position after 15 minutes of rest [2]. The equipment has been validated in children [34]. The mean of three measurements was used in all analyses. Pulse pressure (PP) was calculated as SBP-DBP and mean arterial pressure (MAP) as $SBP/3+2DBP/3$ [31].

Echocardiography

Studies were performed with 2-dimensional guided M-mode echocardiography obtained in the parasternal short and long-axis views, in accordance with the recommendations by the American Society of Echocardiography [28]. The following variables were measured: End-diastolic left ventricular diameter (LVDD), left atrial end-

systolic diameter (LA), end-diastolic inter-ventricular septum thickness (IVS), end-diastolic posterior wall thickness (PW). Left ventricular mass (LVM) was calculated using the ASE convention; $LVM = 0.83 \times [(LVDD + IVS + PW)^3 - LVDD^3] + 0.6$ (measurements in cm) [28]. Both LA and LVM were indexed for height [23, 29, 32]. Relative wall thickness (RWT) of the left ventricle was calculated as $2 \times PW/LVDD$ [28].

Statistics

Analyses were made in Statistica 7.1, with the exception of logistic regression which was performed in SPSS 18.0. Descriptive statistics include mean \pm standard deviation (SD). Skewed variables were normalised by natural logarithm (ln), values without logarithmic transformation are also displayed. Linear relationships were assessed with Pearson correlation coefficients. Group differences between mean values were tested using the unpaired Student's t-test. Z-scores (value for the individual-mean value for group)/SD were calculated, by sex. Sum of z-scores for DBP, SDP, PP, MAP, RHR, LVM, LA, RWT, BF%, AFM, and AFM/TBF were calculated in boys and girls, separately, and used as composite risk factor score for CVD. One-way ANOVA analyses were used to investigate significant differences in composite risk factor score between the different quartiles of VO_{2PEAK} , with adjustment for sex. In addition, odds ratios for elevated composite risk factor score were calculated between quartiles of fitness using logistic regression, with adjustment of sex. In order to calculate odds ratios, cardiovascular risk was dichotomized at the cut-off value for sum of z-score of plus 1 SD. Statistical significance was set at a level of $P < 0.05$.

Results

Two children were excluded because DXA data were not available, two children did not accept blood pressure measurement because they considered it painful, and one child was excluded because of failure to perform an adequate exercise test. Thus, the final study group consisted of 243 children (boys $n=136$, girls $n=107$), aged 8 to 11 years.

There were no significant differences between boys and girls concerning age, height, total body mass or BMI. Boys had higher VO_{2PEAK} and lower TBF, BF%, AFM, AFM/TBF and RHR ($P < 0.05$) than girls. Furthermore, boys had more LVM, whereas no differences were found for LA, RWT, SBP, DBP, MAP or PP. Summary of anthropometrical, DXA, blood pressure and echocardiography data are displayed in table 1. Five girls were Tanner stage 2, all other children Tanner stage 1.

Significant correlation coefficients existed between VO_{2PEAK} and most individual z-scores for the separate CVD risk factors (Table 2). Significant ($P<0.05$) Pearson correlation coefficients between VO_{2PEAK} and individual z-scores, with adjustment for sex, ranged from -0.13 to -0.59. Moreover, Pearson correlation revealed significant associations between VO_{2PEAK} and composite risk factor score in both boys ($r=-0.48$, $P<0.05$), and in girls ($r=-0.42$, $P<0.05$).

One-way ANOVA analysis indicated significant differences in composite risk factor score between the different quartiles of VO_{2PEAK} ($P<0.001$). Figure 1 shows the findings for boys and girls.

Odds ratios, with 95% confidence interval (CI), for elevated composite risk factor score (using the fittest quartile as referent) were with decreasing fitness in the different quartiles; 2.7 (95% CI 0.7-6.9), 2.2 (95% CI 0.7-6.9), and 14.6 (95% CI 5.1-41.8).

Discussion

The main finding in the present investigation in young children was the relationship between aerobic fitness and clustering of risk factors for CVD. The finding is of interest, even if we must emphasise that the cross-sectional nature of the present study can only present potential relationships, and not address what is cause and effect.

The composite risk factor score used in the present investigation was constructed from a number of separate risk factors for CVD, such as LA [23, 32], LVM [29], RWT [16], SBP, DBP, MAP, PP [8, 31], RHR [22], and body fat measurements [27]. All these individual risk factors have been shown to be independent predictors of outcome in adults and it is reasonable to suggest that they represent surrogate markers for cardiovascular health [8, 16, 22, 23, 27, 29, 31, 32]. Much of the correlation between VO_{2PEAK} and the composite risk factor score for CVD in the current study was caused by the body fat measurements. VO_{2PEAK} was, however, in univariate analyses related to the majority of single risk factors. The correlation coefficients that were not significant were all in the hypothesized direction, with exception of RHR. The non-significance for some of these relationships could be attributed to limited sample size. The principal purpose, however, of the current analyses was to investigate the relationship between VO_{2PEAK} and composite risk factor score for CVD. The accumulation of these risk factors, if started in early childhood and sustained during a long time is believed to have greater impact on CVD and mortality than one single risk factor [2, 6]. One could argue that the advantage of a composite risk factor score analysis is that it yields a comprehensive perspective. The disadvantage is that each factor is given equal importance as the sum of z-scores is added together, and there is no evidence base for this assumption.

Moreover, the composite risk factor score is sample-specific and therefore highly dependent on the sample of children studied, making it difficult to compare between studies. We also dichotomized the value for sum of z-scores of +1 SD in order to calculate odds ratios. The assumption that a z-score above 1 SD in a composite index for CVD risk factors actually denotes a risk is an assumption not based on outcome studies in adults. However, most of the available evidence suggests that risks starts to increase below different cut-off points.

There have been several reports on the relationships between fitness, by indirect methods, and multiple other risk factors for CVD in representative samples of young children [3, 4, 7, 19-21, 26]. Data with more comprehensive analyses of the relationship between direct measurement of VO_{2PEAK} and other risk factors for CVD in representative samples of young children are scarce [18, 35-36]. Eiberg et al. investigated 369 children aged 6 to 7-year old [18]. Children in the lowest quartile of fitness had a higher composite risk factor score for CVD compared with the other quartiles. Their composite risk factor score was composed of SBP, DBP, body fat from sum of skinfold measurement, but also blood samples such as triglycerides, insulin, HDL, and HOMA score. Resaland and co-workers recently reported a similar finding, using similar methodology, in 227 children aged 9 years, where the children in the lowest quartile of fitness again had the highest composite risk factor score for CVD [35]. Similar findings were reported for 1592 9-yr-old and 15-yr-old boys and girls after adjustment for age, sex and pubertal status [36]. In this investigation slightly over 50% of the study population consisted of 9-yr-olds. It is, however, not possible to differentiate the CVD risk factor status in the 9-yr-olds from the 15-yr-olds since the results where pooled in the analysis. Our study confirmed the results from the cited studies, but differs in some aspects. MAP, **RHR**, PP, and structural cardiac differences were included in this investigation. Furthermore DXA was used, which is a more accurate method compared to sum of skin folds to estimate body fat. In the current study blood samples were not available, as many of the children did not consent to this. It was therefore not possible for us to include triglycerides, lipoproteins, insulin or other factors that have been shown to predict health outcome into the model. The combined knowledge of our study and previous investigations suggests, however, that approximately 25% of young children exhibit elevated composite risk factor score for CVD in combination with a decreased fitness level.

Major strengths of the present investigation are the reasonably large representative sample of urban children and the objective measurement of body composition. Moreover, direct measurement of VO_{2PEAK} is considered the optimal method for assessment of aerobic fitness since all other methods introduces errors [14]. A limitation of

the present investigation is that DXA is only capable of measuring all the fat in the abdominal region and not to differentiate intra visceral from and extra visceral fat. Furthermore, epidemiological studies in adults that have established different fat measurements as outcome variables have used anthropometric measurements rather than DXA. In addition, there is naturally the possibility of potential collinearity between different risk factors and VO_{2PEAK} . The purpose of the present investigation was, however, to investigate the relationship between VO_{2PEAK} and different risk factors, as they have been established in outcome studies in adults. The only way to do this is to used the same scaling methods (or not to scale) as in the original investigations [8, 16, 22, 23, 27, 29, 31, 32]. We assessed puberty status by self-evaluation according to Tanner because of convenience, which may have misclassified a limited number of subjects. Assessment of puberty status by self-evaluation have however been shown to provide accurate evaluation on a group level [17]. The inclusion frequency in this study of 52% might be considered somewhat low, and the vast majority declined participation without offering any reason which makes fall out analysis difficult. A separate study of anthropometric data from all children that received an invitation to participate in the study showed no significant differences in height, body mass or BMI between the children that chose to participate and those who did not [9]. This suggests that the finding in this study could be generalized.

There are several ways to express the VO_{2PEAK} value. We choose to scale VO_{2PEAK} to body mass, since VO_{2PEAK} has been scaled to body mass in most investigations in adults concerning health outcome. When scaling VO_{2PEAK} to body mass, however, body fat will become an automatic confounder. Previous investigations have made attempts to separate relationships between VO_{2PEAK} and CVD in fit but fat and fat and unfit children [20-21]. We were not able to perform the same analysis due to limited sample size.

In conclusion, the present study in a representative sample of young children observed a moderate relationship between directly measured aerobic fitness and a composite risk factor score for CVD. Our findings are in agreement with the suggestion that improvement in fitness could be of importance as risk factor intervention. Whether improvement in fitness actually leads to reduction in composite risk factor score and subsequent improved outcome remains to be investigated.

Acknowledgements

Financial support for this study was received from the Swedish Heart and Lung Association and Lund University Grants.

Conflict of interests

The authors declare that they have no conflict interests.

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Figure legends

Figure 1

Sum of z-scores, with adjustment for sex, in different quartiles of VO_{2PEAK} ($\pm 95\%$ confidence intervals). Boys and girls in quartile 1 had the highest composite risk factor score for cardiovascular disease (CVD).

Boys and girls (n=243)
Vertical bars denote 0.95 confidence intervals

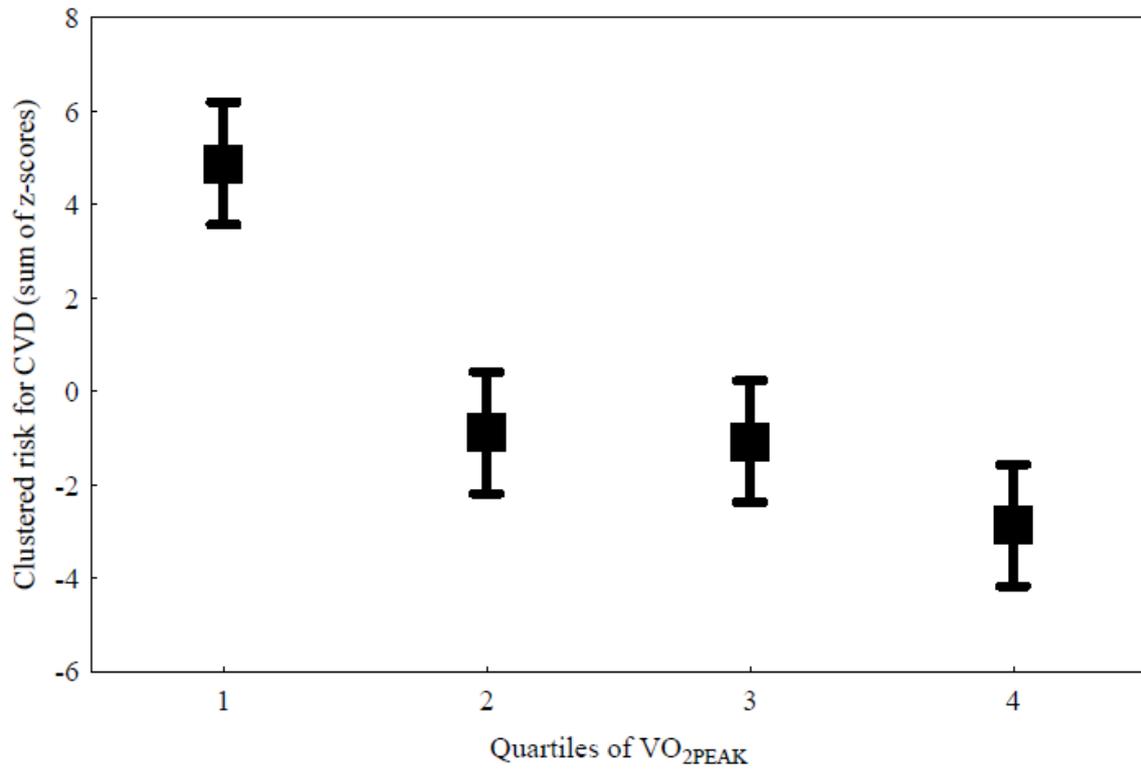


Table 1. Age, anthropometric, DXA, echocardiography and blood pressure data for all children with valid measurements (n=243). Values are presented as mean \pm SD.

Variable	Boys (n=136)	Girls (n=107)	P-value
Anthropometrics and age			
Age (yrs)	9.9 \pm 0.6	9.7 \pm 0.6	0.06
Height (cm)	141.1 \pm 6.8	140.4 \pm 7.8	0.46
Body mass (kg)	35.0 \pm 7.6	34.6 \pm 7.7	0.72
BMI (kg/m ²)	17.4 \pm 2.7	17.4 \pm 2.9	0.98
DXA			
BF% (%)	16.4 \pm 8.6	21.9 \pm 9.0	<0.001
AFM (kg)	2.4 \pm 2.2	3.2 \pm 2.4	0.009
AFM/TBF	0.36 \pm 0.05	0.38 \pm 0.05	0.047
Fitness			
VO ₂ PEAK (ml/min/kg)	41.6 \pm 7.1	35.8 \pm 6.4	<0.001
Echocardiography			
LVM (g/m)	53.1 \pm 12.3	47.3 \pm 11.2	<0.001
LA (mm/m)	20.1 \pm 2.5	19.5 \pm 2.0	0.07
RWT	0.30 \pm 0.06	0.30 \pm 0.06	0.81
Blood pressure			
SBP (mm Hg)	104 \pm 8	104 \pm 9	0.97
DBP (mm Hg)	59 \pm 6	61 \pm 6	0.13
MAP (mm Hg)	74 \pm 5	75 \pm 7	0.30
PP (mm Hg)	45 \pm 8	44 \pm 7	0.21
RHR (beats/min)	80 \pm 11	85 \pm 10	<0.001

Abbreviations:

Percent body fat (BF%), abdominal fat mass (AFM), body fat distribution (AFM/TBF) , maximal oxygen uptake (VO_{2PEAK}), left ventricular mass (LVM), left artial end-systolic diameter (LA), relative wall thickness (RWT), systolic blood pressure (SBP) and diastolic blood pressure (DBP), pulse pressure (PP), mean arterial pressure (MAP), and resting heart rate (RHR).

Table 2. Pearson univariate correlation coefficients for boys and girls (n=243) combined (with adjustment for sex) between maximal oxygen uptake (VO_{2PEAK}) versus z-scores for the individual risk factors (*P<0.05). Percent body fat (BF%), abdominal fat mass (AFM), body fat distribution (AFM/TBF), left ventricular mass (LVM), left artial end-systolic diameter (LA), relative wall thickness (RWT), systolic blood pressure (SBP), diastolic blood pressure (DBP) , mean arterial pressure (MAP), pulse pressure (PP), and resting heart rate (RHR).

	VO_{2PEAK}
BF%	-0.58*
AFM	-0.59*
AFM/TBF	-0.42*
LVM	-0.16*
LA	-0.10
RWT	-0.12
SBP	-0.14*
DBP	-0.10
MAP	-0.13*
PP	-0.08
RHR	-0.00