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Normal values for cardiopulmonary exercise testing in children

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Abstract

Background: A reference set of data of normal values of newly developed cardiopulmonary parameters of exercise testing in an 8-18-year-old population is lacking.

Patients and methods: Cardiopulmonary exercise testing was performed in 175 healthy school children (8-18 years old). Continuous electrocardiography was performed, and minute ventilation, oxygen uptake (VO_2), and carbon dioxide (CO_2) production were measured continuously with a respiratory gas analysis system.

Results: Peak VO_2/kg did not change with age, whereas the ventilation to carbon dioxide exhalation slope was lower in the older children. The decline in heart rate during recovery was much faster in the youngest children. Linear regression analysis showed a significant effect of age on: peak work rate (WR_{peak}) and WR_{peak}/kg, ventilation to carbon dioxide exhalation slope, heart rate recovery, and VO_{2peak} (boys only) (All $P < 0.001$). The $\Delta VO_2/\Delta WR$ slope remained constant throughout all age groups.

Conclusion: This study comprehensively provides a reference set of data for the most important cardiopulmonary variables that can be obtained during exercise testing in children.

Keywords

Cardiopulmonary, exercise testing, healthy children

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Introduction

Cardiopulmonary exercise testing (CPET) is frequently used as a tool for evaluating chronic condition,[1] including congenital heart disease (CHD) in children.[2,3] Currently, most children who have undergone surgical or interventional treatment for congenital heart defect nowadays survive till adulthood. However, residual defects or problems resulting in decreased exercise capacity often occur relatively. Many cardiopulmonary variables may contribute to a reduced exercise tolerance, including systolic and diastolic ventricular dysfunction, sinus node dysfunction, and changes in cardiac autonomic nervous activity, whereas reduced physical activity in these patients may further lead to reduced exercise tolerance.[4] Physical training at recommended levels may increase exercise tolerance,[5,6] while the use of different cardiopulmonary parameters in the evaluation of exercise tests may give more insight into the mechanisms of reduced exercise tolerance. These parameters include simple measures as peak work rate (WR_{peak}) and heart rate (HR) response to exercise, peak oxygen uptake (VO_{2peak}), and more recently proposed measures as the ventilation to carbon dioxide exhalation (VE/VCO_2) slope. Some of these parameters lack normal values for the pediatric population. Moreover, published reference values might not be representative for today's children.[7–10] Equipment for CPET has evolved from the Douglas bag technique to breath-by-breath analysis of expired gases.[11] Furthermore, important changes have occurred in

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body weight and activity level of children in the industrialized countries.

To obtain reference data for exercise testing, we investigated the CPET results of 175 healthy Dutch school children with an age range of 8-18 years.

Methods

The study population consisted of 175 healthy school children. They were recruited from a primary school (8-12 years old) and a secondary school (12-18 years old) from the city of Rotterdam. The study was approved by the Institutional Review Board of Erasmus University Medical Center, Rotterdam, The Netherlands, and written informed consent was obtained from the legal guardians and from the children if appropriate. Sporting activities were performed only at a recreational level. All children came to the hospital by car, or, they came by bike or walking if their residence was within 10 min away from the hospital.

Exercise testing was performed in the upright position with a cycle ergometer (Jaeger ER9000; Viasys Healthcare, Hoechberg, Germany). Breath-by-breath respiratory gas analysis was performed using an Oxycon Champion System (Viasys Healthcare). WR was increased stepwise with 15 or 20 W/min according to length. Children shorter than 150 cm underwent a protocol with 15 W/min increment, a 20 W/min increment was used in the taller children. Participants began exercise testing by cycling at 0W (unloaded) WR with a minimum of 3-min warm-up phase. All participants were verbally encouraged to exercise to exhaustion, as assessed using a cut-off greater than 1.01 for the respiratory exchange ratio (RER) at peak exercise. After maximal exercise has been reached, a cooling down phase consisted of 5 min pedaling at a slow rate (<40 revolutions/min) at a WR of 0W. All equipments were calibrated according to the instructions of the manufacturer before testing. HR was measured by continuous 12-lead electrocardiography.

VO_{2peak} was defined as the mean of the two highest consecutive values of 15-s averages of VO_2. The VE/VCO_2 slope was obtained by linear regression analysis of the data acquired throughout the entire period of exercise.

Resting HR was measured after at least 3 min in a seated position before exercise testing, and peak HR (HR_{peak}) was defined as the highest HR achieved during exercise. HR reserve was calculated as the difference between HR_{peak} and resting HR. HR was also recorded 1 and 2 min after the cessation of the exercise, and HR recovery was calculated as the difference between HR_{peak} and the HR at these recovery points. The relative decrement in HR was calculated as ((HR_{peak}-HR recovery)/HR reserve)* 100%. WR_{peak} was measured in absolute values and also in W/kg. VO_2 was plotted against VCO_2, and ventilatory threshold (VT) was determined as a sudden rise in VCO_2 in excess of VO_2,[8] and was expressed in ml/kg per min and also in percentage of VO_{2peak}. VO_2 versus WR ($\Delta VO_2/\Delta WR$) was measured as the slope as obtained by linear regression analysis of VO_2 (ml/min) versus WR (W).

Statistics

Statistical analysis was performed with SPSS 11.5 (SPSS, Inc., Chicago, Illinois, USA). Values are presented as mean ± standard deviation unless stated otherwise. A two-sample *t*-test was used to compare the means of continuous variables with a normal distribution, and Mann-Whitney test for continuous variables without normal distribution. Categorical values were compared using the χ^2 test or Fisher exact test. Linear regression analysis was used to determine VE/VCO_2 and $\Delta VO_2/\Delta WR$. The effect of age on the measured parameters was determined by linear regression analysis as well. A P value less than 0.05 was considered statistically significant.

Results

The study population consisted of 175 children (93 boys, 82 girls) with an age range of 8–18 years (mean 12.5 ± 2.9). Mean height and body mass were 157 ± 15 cm (range 124–197) and 47 ± 14kg (range 25–81), respectively (Tables 1 and 2; Figure 1). Comparison of body height and weight with a Dutch reference population showed Z-values of 0.13 ± 0.94 and 0.16 ± 0.82, respectively.[12] Thirteen children (six boys) had a body mass index (BMI) greater than 90th percentile.

All participants performed the cardiopulmonary exercise test without complication and were able to complete the protocol to volitional exhaustion. A 15 W/min increment was used in 68 children, in the other 107 children, 20W/min increment was used. The exercise duration was 8 ± 2 min. No electrocardiography abnormalities were noted during exercise testing. HR_{peak} and HR reserve did not change with age. Compared with girls, boys reached a higher W_{peak}, and had a higher VO_{2peak}/kg.

Linear regression analysis showed a significant effect of age on W_{peak}, W_{peak}/kg, VE/VCO_2 slope, and HR recovery for boys and girls and for VO_{2peak} for boys only (Figures 2–5). The corresponding regression equations are given in Table 3. All were significant at P values less than 0.001. Thirteen children with an increased BMI had a lower VO_{2peak} (38 ± 4.8 ml/kg

Table 1. Baseline characteristics in boys and girls according to different age groups

Age (years)	8–9	10–11	12–13	14–15	≥16
Boys					
Number[a]	21	24	20	7	21
Length (cm)	138 ± 5	151 ± 7	159 ± 6*	172 ± 9	182 ± 8***
Weight (kg)	33 ± 5	40 ± 7	46 ± 8	56 ± 13	68 ± 8***
Body mass index (kg/m^2)	17.1 ± 1.7	17.6 ± 2.1	18.0 ± 2.9	18.9 ± 2.8	20.4 ± 1.9
Girls					
Number[a]	20	21	21	8	12
Length (cm)	140 ± 8	152 ± 8	164 ± 7	168 ± 6	169 ± 4
Weight (kg)	35 ± 11	41 ± 6	52 ± 12	56 ± 8	60 ± 7
Body mass index (kg/m^2)	17.5 ± 3.2	17.7 ± 2.0	19.1 ± 4.1	19.8 ± 2.3	21.0 ± 2.5

[a]Number of controls. *$P < 0.05$ for the difference between boys and girls. ***$P < 0.001$ for the difference between boys and girls.

Table 2. Cardiopulmonary exercise data in boys ($n = 93$) and girls ($n = 82$)

	Boys	Girls
Number[a]	93	82
Height (cm)	158 ± 17	156 ± 13
Weight (kg)	47 ± 15	46 ± 13
Body mass index (kg/m^2)	18.3 ± 2.5	18.7 ± 3.2
HR_{peak}	184 ± 12	186 ± 10
W_{peak}	162 ± 65	142 ± 44*
VO_{2peak}	47 ± 7	42 ± 6***
VE/VCO_2	30 ± 4	31 ± 4
RER_{peak}	1.13 ± 0.08	1.14 ± 0.09
HR reserve	104 ± 15	100 ± 13
HR01 percentage	0.35 ± 0.13	0.32 ± 0.11
HR02 percentage	0.54 ± 0.11	0.51 ± 0.12
VO_2AET	28 ± 2	26 ± 5
VO_2 percentage AET	61 ± 11	62 ± 10
$\Delta VO_2/kg/\Delta WR$	0.23 ± 0.07	0.29 ± 0.04
$\Delta VO_2/\Delta WR$	9.9 ± 0.9	9.3 ± 1.0
W_{peak}/kg	3.4 ± 0.6	3.1 ± 0.5***

HR_{peak}, maximal heart rate at peak exercise (beats/min); HR reserve, maximal heart rate - resting heart rate (beats/min); HR01 percentage, percentage heart rate recovery at 1 min $(HR_{max}-HR_{present})/(HR_{max}-HR_{rest})*100^{\%}$; HR02 percentage, percentage heart rate recovery at 2 min $(HR_{max}-HR_{present})/(HR_{max}-HR_{rest})*100\%$; RER_{peak}, maximal respiratory exchange ratio; VE/VCO_2, slope of respiratory minute volume to CO_2 production; VO_2AET, oxygen uptake at anaerobic threshold (ml/kg per min); VO_2 percentage AET, (VO_2 at anaerobic threshold/ VO_{2max})*100%; VO_{2peak}, maximal oxygen uptake (ml/kg/min); ΔVO_2/ kg/ ΔWR, slope of work rate (W) to oxygen uptake (ml/kg per min); $\Delta VO_2/\Delta WR$, slope of work rate (W) to oxygen uptake (ml/min); W_{peak}, maximal work rate achieved (W); W_{peak}/kg, W/kg at peak exercise. [a]Number of controls. *$P < 0.05$ for the difference between boys and girls. ***$P < 0.001$ for the difference between boys and girls.

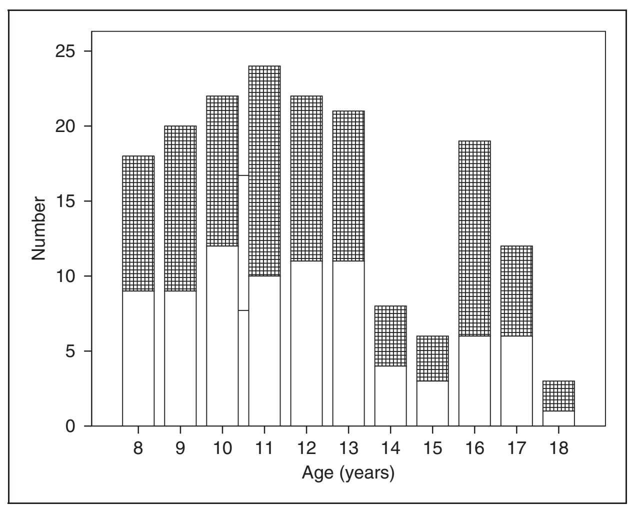

Figure 1. Age and sex distribution of the study population is shown. The hatched area represents boys, girls are represented by the white area.

per min) as compared with the other children (45.2 ± 7.2 ml/kg per min, $P < 0.01$). When expressed in absolute values (ml/min) this difference disappeared. All other values were similar between the two groups.

Discussion

The primary aim of this study was to provide cardio-pul-monary reference values for exercise testing with bicycle ergometry in a contemporary cohort of healthy children between 8 and 18 years of age. There was a significant effect of age on HR recovery and VE/VCO_2 slope, whereas age did not have an effect on HR reserve. VO_{2peak}/kg and W_{peak} were significantly

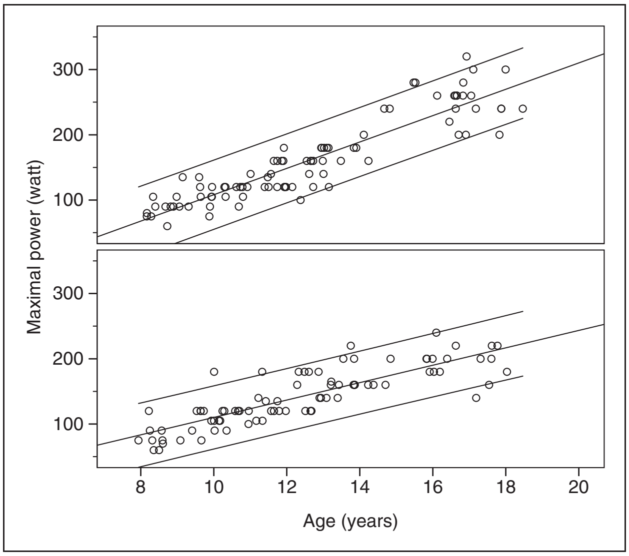

Figure 2. The relation between age and the maximal work rate for the individual participants is shown. The mean value and the 95% confidence limits of work rate related to age are shown. As the difference between boys and girls is significant the results for boys (upper panel) and girls (lower panel) are given separately.

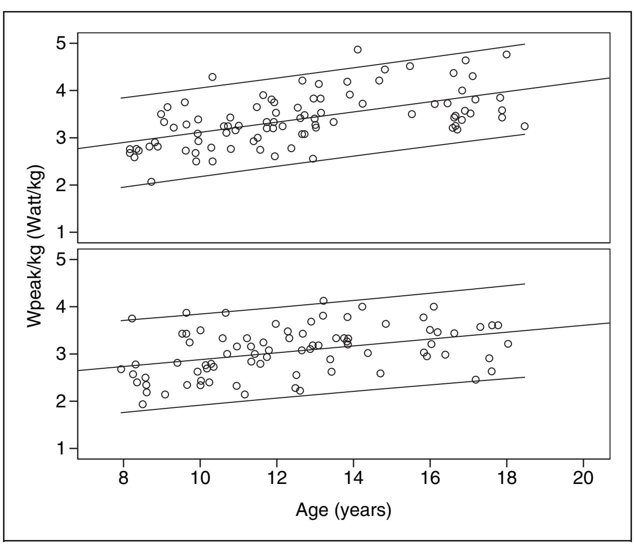

Figure 3. The relation between age and the power/kg for the individual participants is shown. The mean value and the 95% confidence limits of power/kg related to age are shown. As the difference between boys and girls is significant the results for boys (upper panel) and girls (lower panel) are given separately.

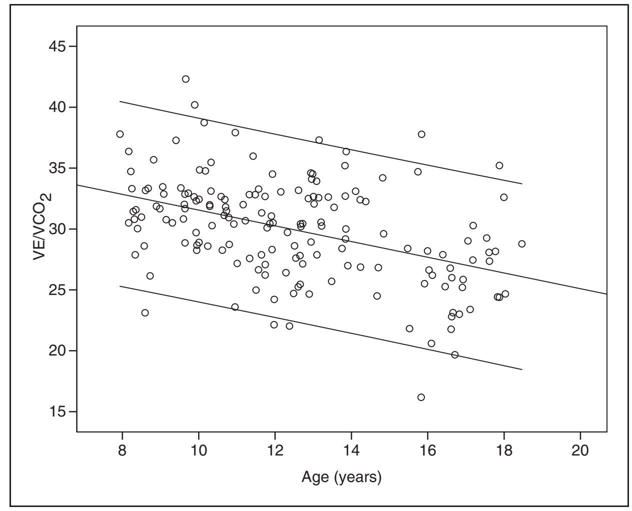

Figure 4. The relation between age and the ventilation to carbon dioxide exhalation (VE/VCO_2) slope for the individual participants is shown. The mean value and the 95% confidence limits of VE/VCO_2 slope related to age are shown.

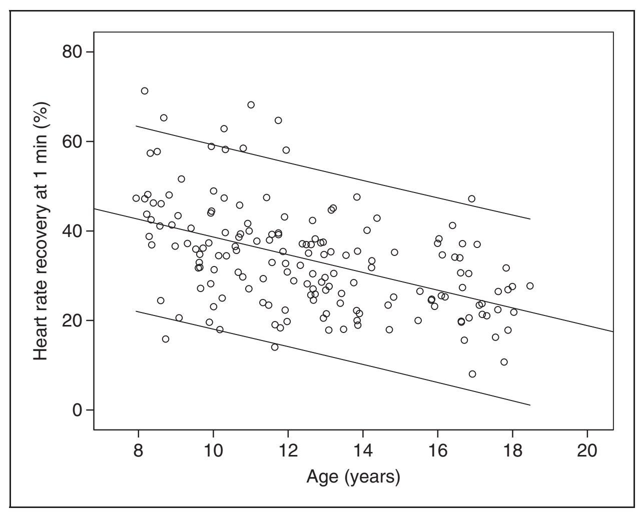

Figure 5. The relation between age and the heart rate (HR) recovery at 1 min for the individual participants is shown. The mean value and the 95% confidence limits of HR recovery at 1 min related to age are shown.

influenced by sex, and this effect was more prominent at older ages. Regression equations for age dependent variables are given for boys and girls separately, which makes it possible to use these values as reference data.

The VE/VCO_2 slope has been studied in patients with congenital heart defects by Dimopoulos et al.[13] These authors showed this variable to be the only predictor of death in a group of adults with CHD.[13] An increase of this variable has been attributed to maldistribution of pulmonary blood flow with increased physiological dead space ventilation. The values obtained in this study are higher when compared with their normal values, although this difference is less prominent in our older children. This age effect has

Table 3. Regression equations for all variables that are age dependent

	SE	r
Boys		
$W_{peak} = (20*age) - 94$	26	0.91
$VE/VCO_2 = (-0.64*age) + 38$	3.6	0.46
HR01 percentage $= (-2.16*age) + 63$	11.0	0.50
$VO_{2peak} = (0.66*age) + 38.6$	7.0	0.27
$W_{peak}/kg = (0.11 *age) + 2.04$ Girls	0.47	0.56
Girls		
$W_{peak} = (13*age) - 23$	24	0.84
$VE/VCO_2 = (-0.64*age) + 38$	4.0	0.40
HR01 percentage $= (-1.84*age) + 55$	9.2	0.49
$W_{peak}/kg = (0.07*age) + 2.16$	0.48	0.39

The equations for boys and girls are given separately. All equations are significant at $P < 0.001$. No significant relation was found between age and VO_{2peak} for the girls. HR01 percentage, percentage heart rate recovery at 1 min $(HR_{max} - HR_{present})/(HR_{max} - HR_{rest})*100\%$; SE, standard error of the mean; VE/VCO_2, slope of respiratory minute volume to CO_2 production; VO_{2peak}, maximal oxygen uptake (ml/kg per min); W_{peak}, peak work rate achieved (W); W_{peak}/kg, W/kg at peak exercise.

been investigated before, and the decrease in VE/VCO_2 slope with advancing age has been explained by a slightly lower pressure of CO2 set point during exercise in the younger children,[14] and higher breathing efficiency in older children (e.g. larger tidal volumes and a relatively lower breathing frequency).

A relatively new parameter in children with CHD is the relation between $\Delta VO_2/\Delta WR$ slope.[15,16] Calculation of the steepness of this slope is a valid measurement of O_2 flow or utilization in the exercising tissues.[17] We found a value of approximately 9.5 ml O2/min per W, irrespective of age, which compares with earlier findings in healthy children.[17] In patients after surgical repair for CHD this value may be reduced, and this may be considered as a factor limiting exercise capacity as it reflects impaired O_2 delivery to the exercising muscles.[15]

VT has been shown to be a useful submaximal parameter in children.[18] Furthermore, it is a good indicator of exercise capacity in children who are unable to perform to maximum exhaustion.[19] The observed values in this study compare well with VT values reported earlier,[8,20] with a VToccurring at 66% of VO_{2peak} in tne 8 and 9-year old children and approximate 60% of VO_{2peak} in the oldest age group.

The value for VO_{2peak} increased with age in only boys (Table 3). A lower VO_{2peak} in girls in older age groups has usually been attributed to the effect of increased body fat.[21] This sex difference is present during adulthood as well.[22] In heart failure patients, VO_{2peak} is probably the best single predictor of survival in ambulatory heart failure patients.[23] Gas exchange analysis performed during exercise has been shown to allow differentiation of children with heart failure from healthy children.[24] Both a lower VO_2 and an increased VE/VCO_2 slope have been found.[24]

If more advanced measurements are not available, the measurement of HR during exercise is simple and inexpensive. A blunted HR response to exercise has been related to diminished exercise capacity[25] while lower HR reserve has even been related to a higher mortality risk in these patients.[25] Factors influencing HR_{peak} in children are intrinsic sinus node dysfunction, and impaired sympathetic cardiac autonomic nervous activity[26] as well as the mode of exercise (e.g. running provides a somewhat higher HR_{peak} compared with cycling). The values of HR_{peak} we obtained were 5 beats/min lower as compared with earlier studies.[7,27] It seems, however, unlikely that our participants did not reach a phase of maximal exercise, as maximal RER was as high as 1.14 on average. A somewhat lower HR_{peak} does not invalidate the exercise parameters obtained in a child. Schulze-Neck et al.[28] found that VO_{2peak}/kg values were comparable in children who achieved a HR_{peak} greater than 180 bpm compared with children with a HR_{peak} lower than 180 bpm.

In our study we found a HR recovery after 1 min of 30–40%. This corresponds to earlier studies in children.[26,27] HR recovery is believed to be mainly influenced by vagal autonomic activity, BMI, and fitness.[27] This makes the HR recovery a good indication of vagal tone, and it has been shown to be a useful marker for evaluating patient outcomes in cardiac rehabilitation in children with CHD.[29] Cardiac autonomic nervous activity has also been shown to be useful in stratifying mild and severe heart failure in pediatric heart failure patients.[30,31] This study showed a faster HR recovery in the youngest children. This confirms results of earlier studies showing a more rapid decline in HR after cessation of exercise in younger children.[27,32] However, results of other measures of vagal activity are equivocal. The high frequency component in HR variability has found to be lower in older children, indicating lower vagal tone from 12 years onwards.[32,33] However, other studies found the highest values of cardiovagal autonomic function in older children, which is most likely a result of maturation of neural mechanisms, attaining peak level at adolescence.[34] Anyway, HR recovery has been shown to be a strong predictor of survival in adults.[35]

Limitations

We studied healthy school children, who actively accepted the invitation to perform exercise testing. This procedure may have lead to bias towards active, nonobese children.[36] However, none of the participants performed dedicated exercise training programs. Furthermore, height and weight of these children were neither different from those in earlier American[7] or Dutch[37] studies, nor did they differ from the values obtained in the population-based Dutch growth study that was conducted in 1997.[12] In this study we used an peak RER (RER_{peak}) of greater than 1.01 as cut-off value. Although an RER_{peak} greater than 1.1 is generally accepted as a threshold for maximal exercise in adults, most studies in children use a threshold of greater than 1.0.[38,39] Furthermore, no correlation has been found in children between RER_{peak} and other measures of maximal exercise as the HR_{peak} or reaching a VO_2 plateau.[39] When data from earlier publications were compared with ours, values for HR reserve and VO_{2peak} were comparable.[7,27,28]

Conclusion

This study comprehensively provides a reference set of data for the most important cardiopulmonary variables that can be obtained during exercise testing in children. VE/ VCO_2 slope decreased with age, suggestive of a more effective gas exchange with advancing age. The faster HR recovery in the younger participants suggests a more active cardiovagal autonomic activity with younger age. The rather uniform value of the $\Delta VO_2/\Delta WR$ slope through all age groups makes it a potential valuable marker of exercise capacity in longitudinal studies. Regression equations for age dependent variables for boys and girls separately are presented, providing a reference dataset.

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