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Open field stress testing: finally an optimal method in young children? Reference values for mobile cardiopulmonary exercise testing in healthy children aged 4–8 years

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Abstract

Introduction: Cardiopulmonary exercise testing represents the diagnostic tool for determining cardiopulmonary function. Especially in small children, exercise testing is extremely challenging. To address this problem, field testing has been implemented using small mobile devices. This study aims at using this protocol for developing normal values for cardiopulmonary exercise testing in very young children. *Material and methods:* Healthy children aged 4–8 years were recruited. All children were tested according to an outdoor protocol, in which they were instructed to walk, then run slowly, then a little harder and at last run at full speed. Each step lasted for 2 minutes, except the last step, in which the children were instructed to maintain as long as possible. *Results:* A total of 104 children (64 female/35 male, mean age 6.6 years) performed outdoor cardiopulmonary exercise testing using a mobile device. Almost all tests were completed successfully (95%). Despite a predominance of female study subjects, anthropometric values did not differ between boys and girls. $\dot{V}O_2peak$/kg, respiratory exchange ratio, VT1, heart rate at VT1, and time of exercise were also comparable between sexes. Generally, a tendency of higher maximal oxygen uptake could be observed in older children. *Conclusion:* Open field mobile cardiopulmonary exercise testing represents a novel approach in very young children. In this study, we were able to determine normal values of maximal oxygen uptake and OUES/kg for 4–8-year-old children. The method is easy to achieve and safe.

Cardiopulmonary exercise testing is used to determine cardiopulmonary function. Knowledge of the cardiopulmonary function of small children is essential, since peak oxygen uptake ($\dot{V}O_2peak$), a surrogate parameter of cardiopulmonary function, is impaired in children with pathologies like CHD,[1–3] asthma,[4] or cystic fibrosis.[5,6]

When only submaximal cardiopulmonary exercise testing is achieved, the oxygen uptake efficiency slope is a promising indicator of cardiopulmonary fitness.[7,8] It correlates strongly with maximal oxygen uptake.[9,10]. As the oxygen uptake efficiency slope rises with age, an oxygen uptake efficiency slope normalised by bodyweight (OUES/kg) or body surface area is proposed by scholars.[11,12]

In small children, stress testing is particularly challenging. Most bicycle cardiopulmonary exercise devices are designed for children above 120 cm in height. Furthermore, smaller children often lack the strength in their knee extensors to reach full exertion on a bicycle.[13] Although cardiopulmonary exercise testing on a treadmill can be performed in young children, this method also faces several problems in this age group. First, they need to be secured by a harness to prevent injuries. Then, most treadmill protocols[14,15] involve an increasing slope of the treadmill, which leads to the aforementioned limitation of the underdeveloped knee extensors.[16] Even though higher rates of $\dot{V}O_2peak$ are achieved by running on a treadmill than on a cycle ergometer,[14,17] due to activation of more muscle groups,[18] outdoor testing achieves even better cardiopulmonary exertion in young children (Rottermann et al., accepted for publication in European Journal of Applied Physiology). Furthermore, most cardiopulmonary exercise testing on a treadmill is rather long with steps up to 3 minutes, which leads to boredom and demotivation in children.

The field method consists of a short test protocol of 6–8 minutes. Plus, the outdoor test setting allows for the evaluation of children in their natural movement, i.e. running. Mobile cardiopulmonary exercise testing can provide valuable diagnostic information in small children

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Table 1. Subjects' age distribution in children with a successful CPET

	Female						Male					
Age (years)	4.0	5.0	6.0	7.0	8.0	Total	4.0	5.0	6.0	7.0	8.0	Total
Total (n)	11	14	12	12	15	64	4	6	9	6	10	35
Exhaustion achieved + VT2 discernible	9	13	10	11	12	55	3	6	9	6	10	34

who were previously too small to perform bicycle cardiopulmonary exercise testing and lack the motor skills for treadmill testing.[18]

So far, normal values for children younger than 8 years are based on either bicycle testing or small cohorts.[19] This study aims to establish normal values of mobile cardiopulmonary exercise testing using an outdoor 6–8 minute running protocol in healthy young children aged 4–8 years.

Material and methods

Healthy children aged 4–8 years without preexisting conditions were included. Written informed consent was obtained from each child and the respective parent using age-appropriate consent forms. All participants were Caucasian, non-obese, and healthy. The study was approved by the Ethics Committee of the University of Erlangen-Nuremberg (159_19B) and the Herzzentrum Leipzig (063/20-ek).

Before cardiopulmonary exercise testing, a thorough clinical examination was performed to rule out contraindications like an acute infection or other preexisting medical conditions. The mobile cardiopulmonary exercise testing device (Cortex Metamax 3B, Cortex Biophysik GmbH, Leipzig, Germany) was fitted to each child using a backpack that could be adapted according to the size of each child. The smallest respiratory mask (Hans Rudolph, Shawnee, Kansas, USA) was adapted using standard headgear. A Custo ECG 3-lead monitoring was installed. Subsequently, an incremental outdoor running test was performed.

All tests were performed on a flat, even ground, either consisting of gravel or asphalt. A physician accompanied the children for instructions, motivation, and safety monitoring. The outdoor running protocol consisted of 2 minutes of slow walking, 2 minutes of slow jogging, 2 minutes of fast jogging, and a maximum of 2 minutes of maximum speed running, as described previously by Schöffl et al.[16] The children received instructions about the speed of each step before the respective step and were then allowed to set the running speed for each step according to their own capacities. During the fastest stage, children were instructed to run as fast as possible for as long as possible and received verbal encouragement. The speed at the last stage was maintained for as long as possible and for maximum of 2 minutes. The children were allowed to terminate the test if they could not maintain their maximum speed because of fatigue. After the test, followed a recovery period of 3–5-minutes of slow walking.

A trained study nurse was present at the exercise site for monitoring the cardiopulmonary exercise testing recordings.

After test completion, values were analysed using the Metasoft Studio software (Cortex Metamax 3B, Cortex Biophysik GmbH, Leipzig, Germany). Graphs were averaged over 20 data points. The following parameters were recorded constantly over the course of the exercise test: Oxygen uptake ($\dot{V}O_2$) as well as CO_2 elimination ($\dot{V}CO_2$), heart rate, respiratory exchange ratio ($RER = \dot{V}CO_2/\dot{V}O_2$), oxygen pulse ($O_2pulse = \dot{V}O_2/HR$), minute ventilation ($\dot{V}E$) and the time of each test (exercise time). VT1 was calculated using the v-slope method[20] and VT2 was calculated according to Binder et al.[21] Oxygen uptake efficiency slope was displayed as the slope of $\dot{V}O_2$ on the *y*-axis plotted against the logarithm of minute ventilation on the *x*-axis ($\dot{V}O_2 = a * \log \dot{V}E + b$, a representing oxygen uptake efficiency slope in l/minute). All oxygen uptake efficiency slope values were calculated from the onset of cardiopulmonary exercise testing to VT2 and were thus only reported in children having achieved VT2. Physiological criteria for having reached exhaustion included two criteria: peak HR ≥ 195/minute, and/or RER at $\dot{V}O_2peak \geq 1.0$.[22]

Statistical analysis was performed using SPSS V25 (IBM, Armonk, New York, USA). Means of metric datasets were compared using two-sided Welch t-testing.[23] Comparisons of multiple age levels were performed using scatterplots, ANOVA testing and multiple linear regression.

P values of <5% in two-sided tests were considered statistically significant ($p < 0.05$*, $p < 0.01$**).

Results

Patient characteristics

A total of 104 children performed cardiopulmonary exercise testing (CPET). No child was injured during running; no dizziness or cardiopulmonary decompensation was observed. In 5 (5%) children, cardiopulmonary exercise testing had to be terminated early due to technical failure (cardiopulmonary exercise testing data not stored and not displayed in software). Failures were not related to patient inherent factors (like, for example, a severing of cardiopulmonary exercise testing device cords or a lack of fitting mask sizes). Of the remaining 99 children, 97 children were Caucasian, 2 children were of mixed ethnicity (one parent Caucasian/one parent Zanzibarian). Their age distribution is displayed in Table 1. Patient characteristics of children (having completed cardiopulmonary exercise testing successfully and having reached exhaustion) are displayed in Table 2.

CPET data

The anthropometric data as well as the data from the cardiopulmonary exercise tests according to sex are represented in Table 2. There were no significant differences between boys and girls with respect to any of the measured variables apart from $\dot{V}O_2$ at VT2, and the oxygen uptake efficiency slope.

$\dot{V}O_2peak/kg$ and oxygen uptake efficiency slope between five different age groups (4–8 years) were compared using ANOVA. There was a significant difference between the age groups with regards to $\dot{V}O_2peak/kg$ ($p = 0.019$) but not with regards to the oxygen uptake efficiency slope ($p = 0.254$).

Multiple linear regression shows that age and sex are not good predictors of $\dot{V}O_2peak/kg$ ($R^2 = 0.104$). However, $\dot{V}O_2peak/kg$ differs significantly by age groups and has a tendency to rise with age, as depicted in Figure 1. By linear regression, we propose to

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Table 2. Patient characteristics

	Sex		
	Female	Male	p
Age (years)	6.4 ± 1.4 (4.1–8.9)	6.8 ± 1.3 (4.6–8.9)	0.165
Weight (kg)	21.9 ± 4.7 (13.6–34.6)	23.7 ± 5.2 (15.0–36.5)	0.095
Height (cm)	119 ± 10.4 (96–143.8)	123.1 ± 10.3 (101–141)	0.067
BMI percentile[24]	43 ± 27 (1–90)	40 ± 27 (1–97)	0.653
$\dot{V}O_2peak/kg$ (ml·minute^{-1}·kg^{-1})	51.1 ± 5.3 (41– 60)	53.3 ± 5.1 (42.0–62.0)	0.055
O_2 pulse	6 ± 2 (3–9)	7 ± 2 (4–11)	0.099
RER at $\dot{V}O_2peak$	1.13 ± 0.07 (0.99– 1.31)	1.13 ± 0.08 (1.00–1.28)	0.705
$\dot{V}O_2$ at VT1 (l · minute^{-1})	0.55 ± 0.17 (0.23–1.11)	0.62 ± 0.19 (0.38–1.32)	0.076
HR at VT1	134 ± 14 (108–166)	137 ± 21 (98–178)	0.515
$\dot{V}O_2$ at VT2 (l · minute^{-1})	0.96 ± 0.2 (0.55–1.38)	1.12 ± 0.26 (0.68–1.54)	**0.004****
OUES (l · minute^{-1})	1.16 ± 0.25 (0.7–1.6)	1.40 ± 0.37 (0.80–2.20)	**0.002****
Time of exercise (minutes)	7.47 ± 0.68 (6.4–9.67)	7.66 ± 1.04 (4.92–9.98)	0.333
OUES/kg	0.053 ± 0.008 (0.032–0.075)	0.058 ± 0.009 (0.042–0.079)	**0.006****

Values are displayed as mean ± 1 standard deviation (minimum to maximum).
**Indicates p < 0.01.

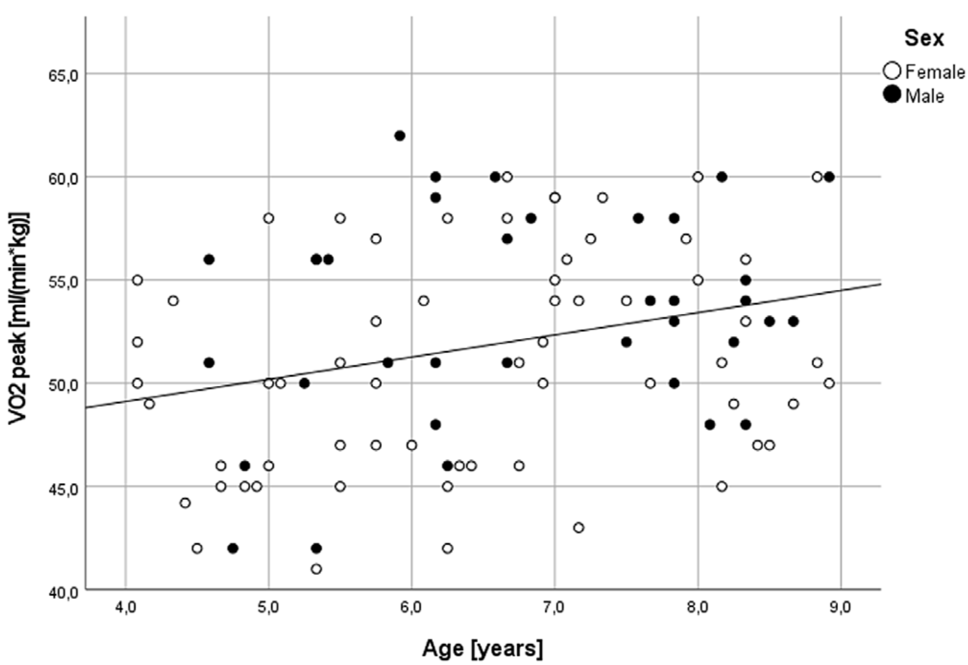

Figure 1. Scatterplot displaying the relation of age, sex and $\dot{V}O_2peak/kg$. One dot represents one child. The graph displays the sole influence of age on Vo_2peak as determined by linear regression.

describe normal values of $\dot{V}O_2peak/kg$ in 4–8-year old children using the following formula:

$$\dot{V}O_2peak[ml^{-1} \cdot kg^{-1}] = 44.814 + age[months/12] \cdot 1.076$$

OUES/kg differs significantly between sexes, but not between age groups.

OUES/kg scattering in different age groups is depicted in Figure 2. We propose to describe mean OUES/kg values as normal values in 4–8 year old children using the following formula:

$$OUES/kg[l \cdot min^{-1} \cdot kg^{-1}] = 0.053 + [female = 0/male = 1] \cdot 0.005$$

Discussion

In this study, we developed normal values for healthy young children performing an 8-minute outdoor cardiopulmonary exercise testing. Outdoor running cardiopulmonary exercise testing can easily be achieved even in very young children, as 95% of tests could be successfully completed. As in earlier mobile outdoor

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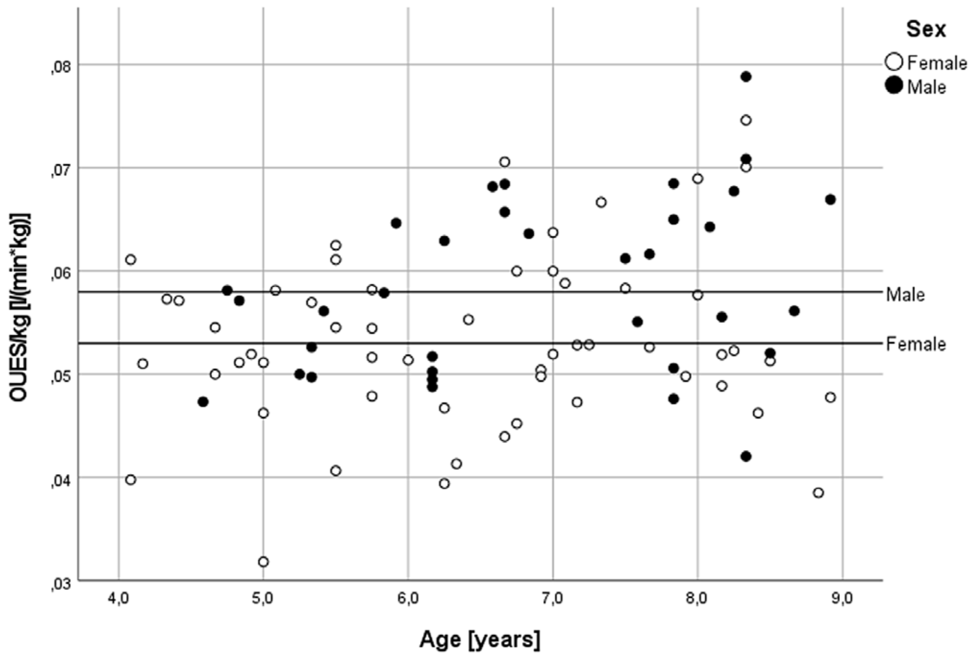

Figure 2. Scatterplot displaying the relation of age, sex and OUES/kg. One dot represents one child. Mean values for boys and girls are displayed.

cardiopulmonary exercise testing cohorts, no child was injured during running; no dizziness or cardiopulmonary decompensation was observed.[16] Therefore, outdoor cardiopulmonary exercise testing in cardiac healthy children can be considered safe.

Despite a predominance of female study subjects, anthropometric values did not differ between boys and girls (Table 2). RER at $\dot{V}O_2peak$, $\dot{V}O_2$ at VT1, O_2 pulse, heart rate at VT1, and time of exercise did also not differ significantly between sexes. Nevertheless, boys reached slightly, yet, significantly higher, $\dot{V}O_2$ at VT2, oxygen uptake efficiency slope, and oxygen uptake efficiency slope normalised to bodyweight values than girls.

The mean $\dot{V}O_2peak/kg$ values recorded in this study are comparable to normal values reported in previous studies in which normal values of children and adults using treadmill cardiopulmonary exercise testing were listed.[15] There was no significant difference between $\dot{V}O_2peak/kg$ of girls and boys in our study. However, there is a significant $\dot{V}O_2peak/kg$ difference between age groups, as shown by ANOVA testing. Taken together and sex are not good predictors of $\dot{V}O_2peak/kg$, as revealed by multiple linear regression ($R^2 = 0.104$). However, in previous literature, a slightly higher $\dot{V}O_2peak/kg$ could be observed in prepubertal boys compared to – girls performing treadmill[25] or bicycle cardiopulmonary exercise testing.[26] This difference in the performance of small children is still a matter of debate. Bodyweight or haemoglobin concentration do not seem to explain $\dot{V}O_2peak/kg$ gender differences in prepubertal children.[25] Increased stroke volume[26] or increased arterio-venous difference[27] were observed in prepubertal boys during cardiopulmonary exercise testing which could result in higher $\dot{V}O_2peak/kg$ values.

We propose to describe normal values of $\dot{V}O_2peak/kg$ in our group by age, as we observed significant difference between age groups. A formula is displayed in Results section.

The oxygen uptake efficiency slope promises to be a reliable indicator of cardiopulmonary fitness, even in submaximal cardiopulmonary exercise testing. Non-normalised oxygen uptake efficiency slope increases with age. Thus, a normalisation to bodyweight or body surface area was proposed by scholars.[10,12] Oxygen uptake efficiency slope and OUES/kg values differed significantly in boys and girls in our study population, suggesting higher values in boys. However, OUES/kg values did not differ significantly between age groups. This suggests constant OUES/kg values regardless of age in children aged 8 years or below. We propose to describe normal OUES/kg in children aged 8 years or below by sex with the formula reported in Results section.

Our OUES/kg mean values were higher than Gavotto's[12] OUES/kg mean values of healthy children determined by cycling cardiopulmonary exercise testing (girls 0.053 vs. 0.0391[12]; boys 0.058 vs. 0.0477 $l{\cdot}minute^{-1}{\cdot}kg^{-1}$)[12] – both $p < 0.001$). However, in the Gavotto population, subjects were older (girls 11.4 ± 2.7, boys 10.9 ± 2.5 years) and had probably partly entered puberty. Higher OUES/kg values in our population might also be explained due to the activation of more muscle groups in outdoor cardiopulmonary exercise testing. In our study, the oxygen uptake efficiency slope was calculated from the onset of cardiopulmonary exercise testing to VT2. In the study by Gavotto et al, the oxygen uptake efficiency slope was recorded from the onset of cardiopulmonary exercise testing to the "maximal point". This may explain higher oxygen uptake efficiency slope values in our population, as we did not determine the oxygen uptake efficiency slope in children who did not reach VT2.

In the future, feasibility of open field cardiopulmonary exercise testing in children with CHD or lung disease is yet to be elucidated. Our group is planning the inclusion of children with CHD into open field cardiopulmonary exercise testing trials. However, sick children can develop severe arrhythmias or cardiopulmonary decompensation during cardiopulmonary exercise testing. This limits a broader application of mobile cardiopulmonary exercise testing in clinical populations, as testing sites would have to be equipped with medical personnel and reanimation equipment readily available.

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Conclusion

This study presents normal values of $\dot{V}O_2peak/kg$ and OUES/kg in a population of healthy 4–8-year-old children. $\dot{V}O_2peak/kg$ means did not differ significantly between sexes but increased in higher age. Mean OUES/kg in boys was significantly higher compared to girls.

Limitations

As the current study did basically include volunteers, the possibility of a selection bias leading to an underrepresentation of sedentary children cannot be ruled out. Almost exclusively Caucasian participants were included, limiting the applicability of results to children from other ethnic groups.

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Conflicts of interest. None.

Ethical standards. Approved by the Ethics Committee of the University of Erlangen-Nuremberg (159_19B) and the Herzzentrum Leipzig (063/20-ek).

Contributorship statement. C. Paech: study design and conduction, critical revision of manuscript. P. Kalden/I. Schoeffl/K. Rottermann: study conduction and paper draft.

F. Markel/A. Michaelis: study conduction and paper revision. S. Brosig/F. Loeffelbein: paper draft. R.A. Gebauer/I. Daehnert: critical revision.

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