Ability of preschoolers to achieve maximal exercise and its correlation with oxygen uptake efficiency slope ~ an observational study by direct cardiopulmonary exercise testing

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Abstract
The oxygen uptake efficiency slope (OUES) is a well-established substitute for maximum oxygen uptake (VO\textsubscript{2max}) in submaximal exercise effort among adolescents and adults. Few studies have analyzed the exercise capacity (EC) and OUES of children aged 4 to 6 (preschoolers). Body fat has been proved to negatively affect EC among schoolchildren. The purposes of this study were to assess the capacity of preschoolers in achieving VO\textsubscript{2max} and evaluate the correlation of peak metabolic equivalent (peak MET) and peak oxygen consumption (peak O\textsubscript{2}) with OUES. We also evaluated if body fat affected EC among preschoolers.

Forty-three preschoolers under the ramped Bruce protocol of treadmill exercise testing had been retrospectively studied. The criteria for achieving VO\textsubscript{2max} included respiratory exchange ratio (RER) > 1.1, heart rate (HR) > 85% of age-predicted maximum, and HR > 200 bpm. OUES was calculated by the 75% (OUES-75) and the entire (OUES-100) duration of the testing and normalized by body surface area. Body fat was measured using vector bioelectrical impedance analysis. The fat mass (FM) index and fat-free mass index (FFMI) were defined as FM or FFM (kg) divided by height squared (m\textsuperscript{2}), respectively.

The mean age of the participants was 5.70 ± 0.56. Seventy-nine percent of preschoolers met at least 1 criterion, 36.84% met 2 criteria, and none met all 3 criteria for VO\textsubscript{2max}. OUES-75 was moderately positively correlated with peak MET (P = 0.034; Spearman’s rho = 0.324) and peak O\textsubscript{2} (P < 0.001; Spearman’s rho = 0.667). OUES-100 was moderately to highly positively correlated with peak MET (P < 0.001; Spearman’s rho = 0.592) and peak O\textsubscript{2} (P < 0.001; Spearman’s rho = 0.825). There were moderate to high positive correlations between FFMI and peak O\textsubscript{2} (P < 0.001; Spearman’s rho = 0.668), OUES-75 (P < 0.001; Spearman’s rho = 0.642), and OUES-100 (P < 0.001; Spearman’s rho = 0.670).

None of the preschoolers reached all 3 criteria for VO\textsubscript{2max}. OUES-75 and OUES-100 might be indicators of peak O\textsubscript{2} at submaximal effort. Preschoolers with higher FFMI had better EC during treadmill exercise testing.

Abbreviations: \%FM = percentage of body fat, BMI = body mass index, BSA = body surface area, CPET = cardiopulmonary exercise testing, FFMI = fat-free mass index, FM = fat mass, FMI = fat mass index, HR = heart rate, MET = metabolic equivalent, OUES = oxygen uptake efficiency slope, peak O\textsubscript{2} = peak oxygen consumption, RER = respiratory exchange ratio, VBIA = vector bioelectric impedance analysis, VO\textsubscript{2} = carbon dioxide production, VE = minute ventilation, VO\textsubscript{2} = oxygen consumption, VCO\textsubscript{2} max = maximum carbon dioxide uptake.

Keywords: exercise capacity, fat-free mass index, oxygen uptake efficiency slope, preschooler, treadmill exercise testing

1. Introduction
Maximum oxygen uptake (VO\textsubscript{2max}) is generally considered the gold standard for determining cardiorespiratory fitness and aerobic fitness.\textsuperscript{1} VO\textsubscript{2max} can be reliably measured in adults. Several discussions have focused on whether VO\textsubscript{2max} is reliably measured in young children.\textsuperscript{2,3} and studies have shown that few children demonstrate a plateau in their oxygen consumption (VO\textsubscript{2}) during exercise to volitional fatigue. Consequently, peak oxygen consumption (peak O\textsubscript{2}) is used as a substitute for VO\textsubscript{2max}. A limited number of studies have determined the cardiorespiratory fitness of preschoolers (children aged 4 to 6 years old) by cardiopulmonary exercise testing (CPET) given the smaller body size relative to the testing equipment, the inability to sustain activity to a maximal level, the reduced motivation, and the potentially shorter attention span.\textsuperscript{4}

Considering that preschoolers may not be able to sustain activity to maximal level during CPET,\textsuperscript{4} an indicator that could be measured during submaximal effort to reflect their cardiopulmonary fitness is needed. The oxygen uptake efficiency slope (OUES) estimates the ventilatory efficiency with respect to VO\textsubscript{2}. 

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Steeper slopes indicate a higher ventilatory efficiency.\textsuperscript{[5]} It is now a well-established substitute for VO\textsubscript{2max} in submaximal exercise effort among adults and older children,\textsuperscript{[6]} but few studies have evaluated the properties of UES in younger children.

Childhood obesity, which is a serious public health challenge in various developed and developing countries,\textsuperscript{[7]} may negatively affect physical fitness.\textsuperscript{[8]} It is also associated with adult obesity and impaired health later in life.\textsuperscript{[9]} An increasing number of data suggested that childhood obesity could occur in preschool age.\textsuperscript{[11]} Published data suggested that fat mass index (FMI), which is defined as fat mass (FM) (kg) divided by height squared (m\textsuperscript{2}), is a better indicator of adiposity than body mass index (BMI) and percentage of body fat (%FM).\textsuperscript{[12]} In the recent study of Henriksson et al.,\textsuperscript{[13]} it was observed that higher FMI was associated with poorer cardiorespiratory fitness.

2. Methods

2.1. Ethics

This study was approved by the Institutional Review Board of Kaohsiung Veterans General Hospital (number: VGHKS1.5-CT7-05). It was also conducted at Kaohsiung Veterans General Hospital from January 2011 to February 2017. All patients provided the informed consent from their parents before the body composition measurement and the exercise testing.

2.2. Patients

This was a retrospective cross-sectional study. The participants of this research included preschoolers who underwent exercise testing at Kaohsiung Veterans General Hospital, Taiwan. The inclusion criteria were as follows: preschoolers who (1) aged 4 to 6 years old, (2) completed transthoracic echocardiographic examination and 12-lead electrocardiogram without known significant medical conditions and without detectable cardiovascular disease, (3) understood the steps of treadmill exercise testing, and (4) showed no signs of acute infection or fever 3 days before exercise testing.

All the preschoolers received body composition measurement first and then treadmill exercise testing. The minimum sample size was 37 with type 1 error = 0.05, power = 0.8, and square correlation = 0.25 after calculating by G\textsuperscript{8}Power software (version 3.1.9.2, for Windows).\textsuperscript{[14]} Since no available data presented in preschoolers, the correlation factor we used in the G\textsuperscript{8}Power software was based on a study about body fat and exercise capacity in Taiwan adolescents.\textsuperscript{[15]} All the data of the included preschoolers were reviewed by 1 doctor (K-L LIN, who has experience in CPET for more than 15 years). Since the preschoolers were all from 1 medical center, participants with missing data or with outliers in body composition measurement and CPET were excluded to avoid selection bias. Finally, a total of 43 preschoolers (24 boys and 19 girls) were recruited after chart review.

2.3. Treadmill exercise testing

According to the American College of Sports Medicine (ACSM) guideline\textsuperscript{[16]} and clinical experiences,\textsuperscript{[17]} treadmill exercise testing is possible in children from the age of 3; exercise testing should be performed with a rope and guided by a trained staff to safeguard the child during the test. Before treadmill exercise testing, each preschooler in our study was familiarized with the procedures and equipment used in the test via a demonstrative explanation. The purpose of the test was explained to preschoolers and their families before obtaining an informed consent (verbal consent from preschoolers and written consent from families). A symptom-limited exercise testing, which consisted of a treadmill, a flow module, a gas analyzer, and an electrocardiographic monitor (Metamax 3B, Corpo Biophysik GmbH Co., Germany), was used to measure the preschoolers' exercise capacity. All participants underwent exercise testing according to the ramped Bruce protocol, as suggested by the ACSM. The test was terminated when preschoolers demonstrated subjective unbearable symptoms, when they could no longer continue, or when they attained maximal effort as indicated by the ACSM.\textsuperscript{[11]} VO\textsubscript{2} and carbon dioxide production (VCO\textsubscript{2}) were measured during the test by using the breath-by-breath method. Minute ventilation (VE), blood pressure (BP), and heart rate (HR) were also measured. HR reserve (HRR) was calculated as the difference between HR at 1 minute after testing and maximum HR during testing. Metabolic equivalent (MET), which is considered equivalent to 3.5 mL of oxygen per kilogram of body mass per minute,\textsuperscript{[17]} was calculated after measuring VO\textsubscript{2}. Peak MET was defined as the maximal MET throughout the whole exercise testing. The anaerobic threshold was determined by VE/VO\textsubscript{2} and VE/VCO\textsubscript{2} methods.\textsuperscript{[20]}

The following physiological criteria for reaching VO\textsubscript{2max} were used:

(1) respiratory exchange ratio (RER) > 1.1,
(2) peak HR > 200 bpm, and
(3) HR > 85% of age-predicted maximum.\textsuperscript{[16,21,22]}

The equation \( \text{VO}_2 = a \times \log(\text{VE}) + b \) was used, and the graphic slope of this equation was determined as UES.\textsuperscript{[6]} We calculated UES by the 75% (UES-75) and the entire (UES-100) exercise duration. Given the variable anthropometric changes in children caused by their development, UES was normalized by the body surface area (BSA) as suggested.\textsuperscript{[15]} The BSA was computed using the Haycock equation: \( \text{BSA} = 0.024265 \times \text{Ht}^{0.3964} \times \text{Wt}^{0.5377} \), where Ht represents the height in centimeters, and Wt refers to the weight in kilograms.

2.4. Anthropometry and body composition

Vector bioelectric impedance analysis (VBIA) was used in this study to measure the body composition of preschoolers since it is easier and cheaper to perform than densitometry and dual-energy X-ray absorptiometry and it is more accurate than measuring skinfold thickness and waist circumference in reflecting body fat.\textsuperscript{[21]} We performed VBIA with the bioelectrical impedance vector analysis software by using the resistance-reactance graph method.\textsuperscript{[24]} Zeus 9.9 PLUS (Jawon Medical Co., Ltd., Kungsang Bukdo, South Korea) was used to analyze the body composition...
of the preschoolers. The machine sent a minute electric current and measured the body composition by using personal data that have been saved (height, weight, sex, age, and newly calculated body impedance) via the tetrapolar electrode method (electrodes were located on both hands, both soles of the feet, and both ankles of participants with frequencies of 1, 5, 50, 250, 550, and 1000 kHz and a current of 360 uA). FMI was defined as FM (kg) divided by height squared (m²), and FFMI was defined as FFM (kg) divided by height squared (m²).

2.5. Statistical analysis

SPSS for Windows version 19.0 (Released 2010, Armonk, NY: IBM Corp) was used for all analyses. Continuous data were expressed as mean ± SD and categorical variables were presented as absolute numbers or percentages. Normality and homoscedasticity were checked before each analysis. The chi-square test was used to test for differences in the distribution between categorized variables. The independent t test was used for normally distributed variables, whereas the Mann–Whitney U test was used for non-normally distributed variables for comparison between boys and girls. Given that several variables were distributed non-normally, Spearman’s correlation analysis was used to determine the associations between variables. P value < .05 was considered statistically significant.

3. Results

All participants featured an average age of 5.70 ± 0.56 years old, an average BMI of 15.79 ± 2.38 kg/m², an average FMI of 2.47 ± 1.45 kg/m², and an average FFMI of 13.98 ± 1.77 kg/m². Table 1 presented the age, anthropometric variables, body composition, and pulmonary function of 43 preschoolers. A total of 16.3% of preschoolers (4 boys and 3 girls) met the overweight and obesity definitions of the World Obesity Federation.25 The height of girls was significantly lower than that of boys (P = .025). %FM was significantly higher in girls (P = .038) than in boys. However, boys featured significantly higher FFMI than girls (P = .035).

Table 2 presented the data acquired during treadmill exercise testing. The average peak O₂ and peak MET reached 0.84 ± 0.19 L and 10.85 ± 1.62 METs, respectively. Boys showed significantly higher peak VE, peak systolic BP, OUES-100, and peak O₂ than girls (P = .009, .017, .017, and .025, respectively). No difference was observed in MET at the point of anaerobic threshold, HR at the point of anaerobic threshold, peak MET, peak HR, peak RER, peak diastolic BP, OUES-73, or HRR between boys and girls.

Among 43 preschoolers, 9 (20.93%) failed to meet any criteria, 34 (79.07%) met at least 1 criterion (defined as Group 2), and 10 (23.26%) met 2 criteria for reaching VO₂max during the whole treadmill exercise testing. None achieved all 3 criteria of VO₂max (Table 3).

Table 4 shows the correlation between OUES and peak EC. OUES-75 was moderate positively correlated with peak MET (P = .034; Spearman’s rho = 0.324) and moderately to highly positively correlated with peak O₂ (P < .001; Spearman’s rho = 0.667). A moderate to high positive correlation was observed between OUES-100 and peak MET (P < .001; Spearman’s rho = 0.592) or OUES-100 and peak O₂ (P < .001; Spearman’s rho = 0.825).

As for correlation between body adiposity and cardiopulmonary fitness during exercise testing, we found that FFMI exhibited a moderate to high positive correlation with peak O₂ (P < .001; Spearman’s rho = 0.668), OUES-75 (P < .001; Spearman’s rho = 0.642), and OUES-100 (P < .001; Spearman’s rho = 0.670). Although a negative correlation was observed between FMI and OUES-75 or FMI and OUES-100, no statistically significant correlation was noted (Table 5).

4. Discussions

In our study, 34 (79.1%) out of 43 preschoolers could achieve at least 1 criterion for reaching VO₂max during exercise testing. However, less than one-fourth of the preschoolers could achieve 2 criteria for reaching VO₂max. This percentage was much less than that in the study by Figueroa-Colon et al,21 who showed that more than 98.3% and 86.2% of pre-pubertal girls (7.3 ± 1.3 years old) could meet at least 1 and 2 criteria for reaching VO₂max by the treadmill test, respectively. Two of the 3 criteria for reaching VO₂max that they used were the same as that in this study (RER and predicted HR). Given that previous studies have indicated that only 21%–49% of children will achieve a VO₂ plateau than adults,26 an HR of more than 200 bpm was
selected as suggested by the ACSM,\(^{16}\) rather than a defined plateau of \(\text{VO}_2\) as the third criterion for \(\text{VO2max}\) in this study. On the basis of these findings, we speculated that preschoolers experience more difficulty in achieving \(\text{VO2max}\) than older children.

Considering that most of the children did not regularly engage in strenuous exercise, their bodies were not adapted to achieve \(\text{VO2max}\) than older children, too. Therefore, a reliable indicator that could be measured during submaximal exercise and could reflect \(\text{VO2max}\) consistently is needed. OUES has been proved an objective and noninvasive CPET parameter that requires no maximal effort. It may be indicative of cardiorespiratory fitness during exercise in healthy children aged more than 7 years old.\(^{5,28}\) OUES-100 has been proved to correlate strongly with peak \(\text{O}_2\) in healthy children aged more than 7 years old\(^{25,27}\) and in adults.\(^{29,30}\) Previous results from the validation study of OUES against \(\text{VO2max}\) also revealed that OUES-75 differs from OUES-100 by only 3.2%.\(^{31}\) Therefore, we determined OUES by OUES-75 and OUES-100 in this study. We found a moderate to high correlation between peak \(\text{O}_2\) and both OUES-75 and OUES-100 in preschoolers. These findings may imply that OUES-75 and OUES-100 could indicate the cardiorespiratory fitness of preschoolers at submaximal effort properly and sufficiently.

### Table 2

Performance of treadmill exercise testing in preschoolers.

|                  | All (n = 43) | Boys (n = 24) | Girls (n = 19) | P value\(^1\) |
|------------------|-------------|---------------|----------------|--------------|
| AT MET           | 8.37±1.31   | 8.43±1.44     | 8.20±1.17      | .58          |
| AT HR, bpm       | 151.88±8.80 | 151.75±8.12   | 152.05±9.80    | .91          |
| peak \(\text{O}_2\), L | 0.84±0.19   | 0.90±0.19     | 0.78±0.16      | .025\(^*\)   |
| peak MET         | 10.85±1.62  | 11.18±1.73    | 10.45±1.40     | .15          |
| peak HR, bpm     | 180.79±7.10 | 180.71±6.56   | 180.69±7.91    | .93          |
| peak VE, L       | 25.19±5.02  | 26.92±4.05    | 23.00±5.36     | .009\(^*\)   |
| peak RER         | 1.16±0.10   | 1.16±0.11     | 1.16±0.11      | .89          |
| peak SBP, mmHg   | 142.40±30.11| 152.30±31.37  | 130.42±24.20   | .177\(^*\)   |
| peak DBP, mmHg   | 87.05±21.88 | 87.74±23.41   | 86.21±20.49    | .83          |
| HRR at 1 minute, bpm | 30.75±10.12 | 33.05±9.58    | 27.38±10.30    | .78          |
| OUES-75          | 1.25±0.28   | 1.29±0.32     | 1.23±0.24      | .53          |
| OUES-100         | 1.03±0.27   | 1.11±0.29     | 0.92±0.21      | .017\(^*\)   |

Continuous data were expressed as mean±SD.

AT HR=heart rate at the point of AT, AT MET=MET at the point of AT, AT=anaerobic threshold, DBP=diastolic blood pressure, HR=heart rate, HRR=heart rate reserve at 1 minute after termination of the test, MET=metabolic equivalent, OUES-75=oxygen uptake efficiency slope calculating by 75% of the exercise duration and normalized by body surface area OUES-100, oxygen uptake efficiency slope calculating by the entire exercise duration and normalized by body surface area, peak MET=MET at peak exercise, peak \(\text{O}_2\)=peak oxygen consumption, peak VE=minute ventilation at peak exercise, RER=respiratory exchange ratio, SBP=systolic blood pressure.

\(^1\)Refers to the \(P\) value of an independent test (for normally distributed continuous variables) or Mann–Whitney U test (for non-normally distributed continuous variables) between boys and girls.

\(^*\)P < 0.05.

### Table 3

Number and percentage of preschoolers that met criteria of achieving maximal oxygen uptake in treadmill exercise testing.

| No. of Criteria Achieved: [RER > 1.1, HR > 85% of age predicted maximum, HR < 200 bpm] | All (n = 43) | Boys (n = 24) | Girls (n = 19) |
|--------------------------------------------------------------------------------------------|-------------|---------------|----------------|
| 1 of 3                                                                                      | 24          | 15            | 9              |
| 2 of 3                                                                                      | 10          | 3             | 7              |
| All 3                                                                                      | 0           | 0             | 0              |

HR=heart rate, RER=respiratory exchange rate.

### Table 4

Correlation between oxygen uptake efficiency slope and (1) peak metabolic equivalent, and (2) peak oxygen consumption during treadmill exercise testing in preschoolers.

|                      | Peak MET        | Peak O2         |
|----------------------|-----------------|-----------------|
|                      | Spearman’s rho  | P value         | Spearman’s rho | P value |
| OUES-100             | 0.592           | < .001\(^*\)    | 0.825          | < .001\(^*\)    |
| OUES-75              | 0.324           | 0.034\(^*\)     | 0.667          | < .001\(^*\)    |

OUES-75=oxygen uptake efficiency slope calculating by 75% of the exercise duration and normalized by body surface area OUES-100, oxygen uptake efficiency slope calculating by the entire exercise duration and normalized by body surface area, peak MET=MET at peak exercise, peak \(\text{O}_2\)=peak oxygen consumption.

\(^*\)P < 0.001.

### Table 5

Correlation between fat mass index, fat-free mass index, and cardiopulmonary fitness during exercise testing in preschoolers.

|                  | Peak O2 | Peak MET | OUES 100 | OUES-75 |
|------------------|---------|----------|----------|---------|
| FMII              | 0.104   | −0.139   | −0.076   | −0.006  |
| FFMI              | 0.52    | 0.46     | 0.69     | 0.98    |
| OUES-75           | 0.668   | 0.122    | 0.670    | 0.642   |

FMII=fat mass index, FFMI=fat-free mass index, OUES-100=oxygen uptake efficiency slope calculating by the entire exercise duration, OUES-75=oxygen uptake efficiency slope calculating by 75% of the exercise duration (all the OUES data were normalized by corresponding body surface area), peak \(\text{O}_2\)=peak oxygen consumption.

Upper row: Spearman’s rho.

Lower row: \(P\) value.
Many studies had shown that health-related physical fitness is associated with total and central body fat among preschoolers,[11,13,30] However, most of these studies on preschoolers used indirect measures rather than direct exercise testing for cardiorespiratory fitness. Henriksson et al.[13] noted that higher FFM was associated with better cardiorespiratory fitness (determined by PRETTT-20m shuttle-run test) in children aged 4.48 ±0.15 years old. We observed that FFM presented a moderate to high positive correlation with peak VO2, OUES-75, and OUES-100 in preschoolers. Our research was the first study to analyze the relationship between body fat and cardiorespiratory fitness by using data directly from treadmill exercise testing. Our study results coincided with previous limited studies and showed that preschoolers with higher FFMI, whether in terms of submaximal or maximal effort, would have better cardiorespiratory fitness.

We also observed some interesting gender differences in respect of body adiposity and OUES in this study, such as boys presented higher FFMI and lower %FM than girls. These results were consistent with those of previous studies in preschoolers,[13,30] which might be explained by that boys are suggested gaining relatively more lean mass components than girls during growing period.[13] Boys also featured higher OUES-100 than girls in this study. This finding correlates with study of Bongers BC et al that concluded that absolute OUES values increased with age in boys and girls, with boys attaining higher values.[28] Since limited studies of OUES in preschoolers were available before the completion of this study, more and more studies need to be conducted to explain the difference in the future.

This study features the following limitations. First, the criterion for reaching VO2max during exercise testing was selected according to the ACSM guideline[16] rather than the 1 used in other previous studies[21] because studies of children older than 8 years old have shown that plateauing is unnecessary for obtaining reliable VO2max measurements.[26] However, no present study discussed the criteria for achieving VO2max during exercise testing in preschoolers. Therefore, it is unclear which criteria were suitable for determining whether preschoolers reached VO2max. Second, despite the normally distributed BMI values of the participants, it is unclear whether preschoolers in this study could represent the whole Taiwanese preschooler population because of the absence of current reference values of FMI and FFMI. Lastly, the sample numbers were relatively small, and the participants were only recruited in 1 medical center. The results might not be applied to whole nation.

5. Conclusions

To the best of our knowledge, this study was the first to evaluate the cardiorespiratory fitness of preschoolers aged 4 to 6 years old. We observed that preschoolers encounter more difficulty in achieving VO2max during exercise than schoolchildren. We found that OUES-75 and OUES-100 might be probable indicators of peak MET and peak O2. Since OUES-75 and OUES-100 could be measured during submaximal effort, it is practical to use them in preschoolers clinically. We also observed that preschoolers with higher FFMI had significantly higher aerobic fitness during exercise testing. Future larger cross-sectional studies with a more secure analysis of cardiorespiratory fitness and to assess the association between cardiorespiratory fitness and body fat among Taiwanese preschoolers are warranted.

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