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Brief communication (Original)

Exercise intolerance in obese children and adolescents

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Background: Abnormal lung function has been reported in the obese population and is associated with the severity of obesity.

Objectives: To identify abnormal lung function in obese children and adolescents, and examine the cardiopulmonary response of those who have abnormal lung functions during exercise, and to reveal predictors of exercise intolerance in this population.

Methods: Fifty obese participants aged 8–18 years (56% male; mean age 13.2 ± 2.0 years; mean BMI 33.0 ± 3.6 kg/m^2, mean BMI z score 3.1 ± 0.3) underwent spirometry, lung volume evaluation, and a cardiopulmonary exercise test.

Results: Lung function abnormalities and exercise intolerance because of pulmonary limitations were found in 36% and 74% of the participants, respectively. A comparison of participants with normal and abnormal lung functions revealed a lower breathing reserve and a higher ventilatory equivalent for CO_2 production (V_E/VCO_2) during exercise in those who had lung function abnormalities (18 ± 15 vs 30±10%, P <0.001 and 30.3 ± 3.3 vs 29.6 ± 3.1; P = 0.02, respectively). Exercise intolerant participants had a higher BMI z score compared with those who were not (3.1 ± 0.3 vs 2.9 ± 0.3; P = 0.03). BMI z score ≥ 2.84 had an 80% sensitivity and 67% specificity for predicting exercise intolerance in this population.

Conclusions: Evaluations of lung function and exercise capacity should be included in the follow-up planning for obese children and adolescents. A BMI z score ≥ 2.84 was most sensitive for predicting exercise intolerance in this population.

Keywords: Adolescent, children, exercise intolerance, obese

Obesity is becoming one of the most serious public health problems in the pediatric population [1, 2]. While regular exercises are essential for weight reduction, many studies found decreased lung function and poor exercise performance in obese children [3-14]. Exercise training programs should be designed with an awareness of these limitations in obese individuals. However, whether lung function abnormalities and the degree of obesity that may result in poor exercise performance in this population is not yet clear. We therefore conducted the current study to identify lung function abnormalities and exercise intolerance in obese children and adolescents, and compare the cardiopulmonary response during exercise between those who had normal and abnormal lung functions, and to identify factors predicting exercise intolerance in this population.

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Materials and methods

Subjects

Obese children and adolescents aged 8–18 years who were regularly followed-up at the Nutrition Clinic of King Chulalongkorn Memorial Hospital were enrolled. Obesity was diagnosed using age and sex specific BMI cut-off points for obesity that were derived from a worldwide international study [15], and defined as equivalent to a BMI of 30 kg/m^2 at age 18. Exclusion criteria included conditions that could affect pulmonary function and exercise capacity evaluations. These were cardiovascular diseases, thyroid diseases, musculoskeletal diseases, neuromuscular diseases, chronic lung diseases, asthma, respiratory tract infection during the previous 2 weeks, respiratory distress, desaturation (SpO_2 < 95%) in room air, and poor performance on the pulmonary function

and cardiopulmonary exercise tests (CPET). Our institutional ethics committee approved the investigation. Informed consent and assent were obtained from the participants and their parents before enrollment in the study. All participants were otherwise in good health and did not receive any medical therapy on the day of the test. Histories were taken and physical examinations were conducted by a pediatrician. Each participant underwent a pulmonary function test (PFT) and CPET on the same day under the supervision of a skilled medical personnel.

Pulmonary function study

Spirometry and lung volumes (measured by body plethysmography) were evaluated by a Vmax 6200 Autobox (SensorMedics, Yorba Linda, CA, USA) diagnostic system when the participant was in a resting stage. PFT variables included forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), FEV_1/FVC ratio, forced expiratory flow rate between 25%–75% of vital capacity ($FEF_{25\%–75\%}$), total lung capacity (TLC), residual volume (RV), RV/TLC ratio and functional residual capacity (FRC). All pulmonary function parameters except for FEV_1/FVC and RV/TLC ratio were expressed as a percentage of the predicted value calculated from the normal value for the Asian population (European Respiratory Society 1993, update). Obstructive defect was defined as an FEV_1 < 80% predicted (and/or $FEF_{25\%–75\%}$ < 70% predicted) with FEV_1/FVC < 0.85 [16]. Restrictive defect was defined as a TLC <80% predicted while hyperinflation was defined as an RV > 135% predicted and RV/TLC > 0.35 [16, 17]. Low FRC was defined as an FRC < 80% predicted [17]. Severity of lung function defect was graded in accordance with the American Thoracic Society and the European Respiratory Society (ATS/ERS) criteria [18].

Cardiopulmonary exercise test

The CPET was carried out on a motor driven, electronically controlled treadmill. Exercise capacity was evaluated using a portable ergospirometry system (Oxycon mobile with Integrated 3-lead ECG; Viasys Healthcare, Yorba Linda, CA, USA). A modified Balke protocol was applied [19]. Treadmill velocity started at 2.7 km/hr with 0% elevation and was increased to 4.0, 5.4, and 6.0 km/hr, respectively, every one minute. Elevation was increased from 0% to 4% and then increased 2% every one minute until the elevation reached 20%, or the criteria for exercise termination were met. The duration of the recovery period was a standard 3 minutes (2.7 km/hr and 0% elevation).

Throughout the CPET, the participant was allowed to breathe through a face mask connected to a pneumotachometer used for tidal volume and minute ventilation (V_E) measurement. Inspired and expired gases were sampled and analyzed breath-by-breath using a computerized system (Oxygen Lab manager system, Viasys Healthcare). The data were averaged every 30 seconds and calculated for oxygen consumption (VO_2) and carbon dioxide production (VCO_2). The system was recalibrated before each test with gases of known concentrations. Heart rate was continuously monitored by electrocardiography (Oxycon mobile with Integrated 3-lead ECG; Viasys Healthcare). Oxygen saturation (SpO_2) was recorded using a pulse oximeter (Oxycon mobile with Integrated 3-lead ECG; Viasys Healthcare).

Respiratory exchange ratio (RER) was calculated by dividing VCO_2 by VO_2. The ventilatory equivalent for oxygen consumption (V_E/VO_2) was the minute ventilation required at a given level of oxygen consumption. This was calculated by dividing alveolar ventilation by oxygen consumption. Ventilatory equivalent for carbon dioxide production (V_E/VCO_2) was minute ventilation required at a given level of carbon dioxide production. This was calculated by dividing alveolar ventilation by CO_2 production. Breathing reserve was calculated by using the formula $(1–V_E/MVV) \times 100\%$, while V_E was minute ventilation at the end of the exercise and MVV (maximum voluntary minute ventilation) was calculated by multiplying FEV_1 by 35.

The participant was allowed to exercise until reaching maximum exercise (heart rate ≥85% of maximum heart rate [HR_{max}]; HR_{max} = 220 – age [y] and RER ≥ 1.1) [20] or at least one of the following criteria was met: the participant requested to stop, significant desaturation (decreased SpO_2 ≥ 4% from baseline), cyanosis, cardiac arrhythmia or confusion.

Anaerobic threshold (AT) was defined using the V-slope and ventilatory equivalent methods [21]. The first method identified the AT as the point showing the disappearance of the linear relationship between VCO_2 and VO_2 while the second method identified AT as the point showing the increase in V_E/VO_2 without a simultaneous increase in V_E/VCO_2 [21].

Spirometry was performed at 5, 10, 15, 20, and 30 minutes, after exercise termination. Exercise induced bronchospasm (EIB) was defined as the participant

demonstrating at least a 12% declination of FEV_1 or a 26% decrease of $FEF_{25\%–75\%}$ from the pre-exercise values [22].

Exercise intolerance because of pulmonary limitation was diagnosed if the participant demonstrated at least one of the following at the end of the exercise [23, 24].

1) RER > 1.1 while the heart rate was still less than 85% of HR_{max}
2) Breathing reserve < 20%
3) V_E/VO_2 > 40
4) Evidence of EIB
5) Desaturation ≥4% from baseline

Statistical analyses

To detect a difference in exercise capacity in terms of VO_2 max/kg between the normal lung function and abnormal lung function groups, we used the following formula calculating the sample size:

$$(n/group) = [2\ (Z_{\alpha/2} + Z_{\beta})^2\sigma^2]/(X_1 - X_2)^2$$

Where $\alpha = 0.05$, $\beta = 0.1$, and X_x represented the mean VO_2 max/kg in each group. Because the previous study done by Mainov et al. [9] found that the mean VO_2 max/kg in obese children with normal lung function was 29.2 ± 3.8 mL/kg/min, we hypothesized that obese participants with abnormal lung function had 5 mL/kg/min of VO_2 max/kg lower than those who had normal lung function: the calculated sample size was 12 for each group. However, because the prevalence of abnormal lung function in obese children reported in the previous study was 46% [6], we had to recruit at least 26 obese participants into this study.

Collected demographic data and anthropometric measurements were presented in percentage, mean and standard deviation where applicable. The BMI values were converted to exact z scores using the LMS method, with the formula:

$$Z = [[BMI/\mu]^L - 1]/\lambda\sigma$$

where the μ and σ and λ were age and sex specific parameters using WHO growth reference data [25, 26].

Predicted percentage was calculated for all pulmonary function parameters (as mentioned above), while CPET parameters including VO_2, VCO_2, breathing reserve, V_E/VO_2, V_E/VCO_2, and duration of exercise are presented as mean and standard deviation.

Data was compared between the two groups using a Student *t* test for continuous variables and a Chi-square or Fisher Exact test (where applicable) for categorical variables. The cut-off BMI z score to predict exercise intolerance was determined from a ROC curve. A two-tailed $P < 0.05$ was considered for statistically significant. The analysis was performed using SPSS version 16.0.

Results

Fifty obese children and adolescents (28 boys and 22 girls) were recruited. The mean age was 13.2 ± 2.0 years. The mean body weight, BMI and BMI z score were 84.5 ± 16.6 kg (range 53.0–123.5), 33.0 ± 3.6 kg/m^2 (range 26.3–42.3), and 3.1 ± 0.3 (range 2.4–3.7), respectively. Lung function abnormalities were found in 18 participants (36%). The most common abnormality was decreased FRC (13 cases; 26%). Others were medium to small airway obstruction with significant bronchodilator response (7 cases), mild restrictive lung defect (1 case), and hyperinflation (1 case).

Forty-seven participants completed the CPET satisfactorily. The mean exercise duration was 10.2 ± 4.0 minutes. The mean VO_2 max/kg was 28.0 ± 4.0 ml/min. Twelve participants (26%) reached maximal exercise (HR ≥ 85% HR_{max} and RER ≥ 1.1) uneventfully. The remainder (35 cases, 74%) demonstrated exercise intolerance because of pulmonary limitations. These cases included exercise-induced desaturation (29 cases, 62%), EIB (7 cases, 15%), breathing reserve < 20% (10 cases, 21%), and V_E/VO_2 > 40 (1 case, 2%).

A comparison between those who had normal and abnormal lung function found a lower breathing reserve and a higher V_E/VCO_2 in those who had lung function abnormalities (18.0 ± 15.0 vs 30.0 ± 10.0%, $P < 0.001$ and 30.3 ± 3.3 vs 29.6 ± 3.1; $P = 0.02$, respectively) (**Table 1**). Obese participants who had exercise intolerance had a higher BMI z score than those who did not (3.1 ± 0.3 vs 2.9 ± 0.3; $P = 0.03$). The BMI z score that had the highest sensitivity for predicting exercise intolerance was determined from a ROC curve (**Figure 1**). A BMI z score ≥ 2.84 had a 80% sensitivity and 67% specificity for predicting exercise intolerance in this population.

Table 1. Comparison of clinical data and cardiopulmonary exercise test (CPET) parameters between obese participants who had normal and abnormal pulmonary function tests (PFT) (n = 47)

Clinical and CPET data	Normal PFT (n = 31)	Abnormal PFT (n = 16)	*P*
Male	16 (51.6%)	9 (56.2%)	0.76
Age (year)*	13.4±2.3	13.1±1.5	0.29
BMI z score*	3.1±0.3	3.0±0.3	0.18
CPET parameters at the end of exercise			
VO_2max (ml/kg/min)*	27.8 ±4.0	28.3 ±4.1	0.83
VCO_2 (ml/kg/min)*	30.1 ±4.3	30.7 ±3.7	0.53
V_E/VO_2*	30.1 ±3.3	33.1 ±4.2	0.32
V_E/VCO_2*	29.6 ±3.1	30.3 ± 3.3	0.02
Exercise time (min)*	10.3 ± 4.0	9.8 ±4.2	0.10
Breathing reserve (%)*	30.0 ±10.1	18.0 ±15.0	<0.001

Data were presented as mean ± SD

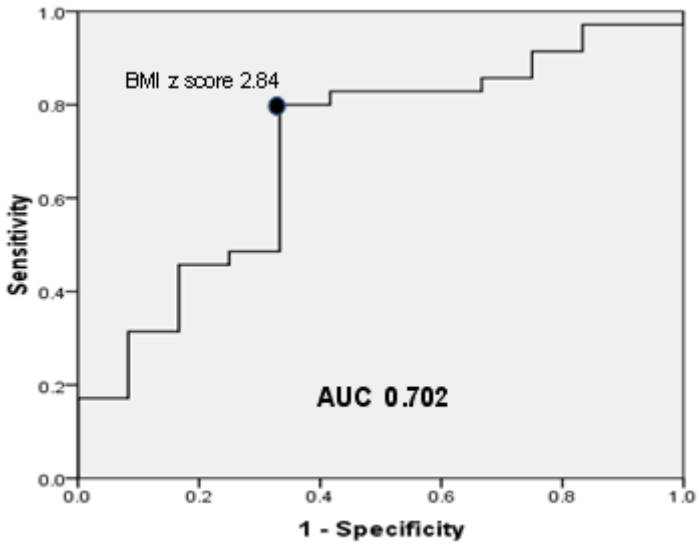

Figure 1. ROC curve showing a BMI z score cut off at 2.84 had 80% sensitivity and 67% specificity for predicting exercise intolerance in obese children with an area under the curve of 0.702.

Discussion

Various lung function abnormalities have been reported in the obese pediatric population [5-8]. In this study, we found abnormal lung functions in 36% of obese children and adolescents. These abnormalities included decreased FRC, obstructive defect, hyperinflation, and restrictive defect, of all which were reported in previous studies [5-8]. The proposed mechanisms of abnormal lung function are impaired lung mechanics secondary to fat deposition in the thoracic cage, airways, and lung parenchyma [4]. Obesity-related inflammation secondary to the production of several adipokines is another possible mechanism of airway inflammation which leads to peripheral airway obstruction, and bronchial hyperresponsiveness including EIB [4, 27-29].

During exercise, the pulmonary system has a role in providing oxygen to the working muscles. In normal individuals, the respiratory system has a sufficient reserve, so it does not limit the exercise. However, if there is lung disease or ventilatory muscle dysfunction, the pulmonary reserve may decrease, and exercise limitation can occur. This is because of the inability of the respiratory system to increase ventilation or

oxygenation with the increasing demand of the body. As was found in this study, many obese participants developed desaturation during exercise, while some demonstrated a decreased breathing reserve and abnormally high minute ventilation for a given level of oxygen consumption (V_E/VO_2). In this study, we found a quite high prevalence of exercise intolerance (74%) in obese children and adolescents. However, the mean BMI z score of the study population was quite high, indicating that most of the study population had moderate to severe obesity. Therefore, the high prevalence of exercise intolerance reported in this study might not be applied to general obese population, especially among those with less severe obesity.

In this study, comparison of the cardiopulmonary response during exercise between those who had normal and abnormal lung functions found a lower breathing reserve, and a higher minute ventilation for any given level of CO_2 production (high V_E/VCO_2) in the latter group. This implied that abnormal lung mechanics limited the ability of the respiratory system to increase the minute ventilation in order to match the increase of metabolic demand during the exercise, and brought about several adverse respiratory events during exercise as were found in this study.

This study also demonstrated an association between the degree of obesity and exercise intolerance. We found a higher BMI z score in those who had exercise intolerance when compared with those who did not. A BMI z score ≥ 2.84 had the highest sensitivity for predicting exercise intolerance in obese children and adolescents. This score may be applied as a screening tool to identify obese individuals at risk for exercise intolerance.

Conclusions

Evaluations of lung function and exercise capacity should be included in the follow-up planning for obese children and adolescents. Exercise training programs for this particular population should be carefully developed by the healthcare workers with an awareness of the possible adverse respiratory events that can occur during and at the end of the exercise, especially in obese children and adolescents who have abnormal resting lung function and a BMI z score ≥ 2.84.

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