Cardiopulmonary Exercise Testing Among Adolescents with Obesity

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Abstract

OBJECTIVE: Cardiopulmonary exercise testing (CPET) is used prior to bariatric surgery in adolescents with obesity to assess surgical risk factors. Lack of normative equations for peak oxygen consumption (pVO2) for this population limits CPET interpretation. We aimed to use lean body weight (LBW) to predict pVO $_2$ and developed novel predictive equations for use in this population. **METHODS:** 446 participants with obesity ages 9-20 underwent CPET prior to bariatric surgery from January 1, 2006 to December 31, 2019. Bioelectrical impedance analysis helped calculate LBW. Achieving peak heart rate > 90% predicted and RER of >1.1 were considered satisfactory effort. **RESULTS:** 107 CPET studies (29%) were satisfactory. Mean weight was 127 ± 21 kg, and BF% 49.7 ± 6.8, and LBW 63 ± 10, kg. Mean pVO $_2$ was 22.2 ± 3.2 mL/kg/min. The mean pVO $_2$ using LBW was 44.8 ± 8.7 mL/kg/min. Total body weight (TBW) estimated pVO $_2$ to be 50.7 ± 7.0 % predicted[(1)](#ref-0001), while LBW estimated it at 102.3 ± 17.6 % predicted. Linear regression yielded reference equations pVO $_2$=1571.6+12.2*TBW (males) and pVO2=1301.8+10.6*TBW (females). **CONCLUSION:** When pVO $_2$ is corrected for LBW, adolescents with obesity demonstrate normal pVO $_2$. A novel set of equations were developed to predict absolute pVO $_2$ using TBW.

Introduction

In the United States, the rate of obesity continues to rise with implications across many if not all organ systems. Today, obesity affects 40% of US adults and 19.3% of US children, totaling 93.3 million adults and 14.4 million children, respectively.(2,3) The vast complications of obesity include strong associations with both the cardiovascular system and the pulmonary system including heart disease, dyslipidemia, asthma, chronic obstructive pulmonary disease, pulmonary embolism and more.(4) Cardiopulmonary exercise testing (CPET) is a useful tool for assessing cardiac, pulmonary, muscular functional status and surgical risk.(5) Several decades of epidemiologic findings have reported that quantified cardiorespiratory fitness (CRF) predicts a positive correlation with better health and lower risk of adverse event post operatively.(6,7)

Evaluating a patient's CPET responses requires that their measured results are compared to predictive values obtained from normative data sets. Peak oxygen consumption (pVO_2) is used to assess reduced exercise capacity and possible cardiorespiratory impairment(8); it is often interpreted standardized across body sizes by dividing the absolute pVO_2 by the patient's kilograms.(9) This method has been found to introduce a bias in adult population(10) and pediatric population with obesity.(10) This has led researchers to develop predicted equations in the adult population for peak VO_2using lean body weight (LBW) instead of total body weight (TBW), given that only skeletal muscle, and not fat, is considered metabolically-active and participating in exercise.(11) Data are limited among the pediatric population for treadmill testing, with a paucity of standardized interpretation among the pediatric population with obesity.(12) The absence of

reference equations for treadmill testing limits interpretation of peak VO_2 in the pediatric population with morbid obesity who are undergoing pre-operative evaluation for bariatric surgical risk.

We aimed to establish normative CPET treadmill data for children with obesity using a large adolescent population with obesity from patients from a bariatric surgery program in New York City. We hypothesized that utilizing LBW data would be a better predictor in estimating corrected peak VO_2 in these patients. We also aimed to develop normal reference regression equations specific to children with obesity using total body mass.

Methods

Participants included all children and adolescents with obesity aged 9-20 years who underwent comprehensive evaluations prior to bariatric surgery at the Center for Adolescent Bariatric Surgery (CABS) at NewYork-Presbyterian/ Morgan Stanley Children's Hospital, Columbia University Irving Medical Center (CUIMC), from January 1, 2006-December 31, 2019 and had undergone a comprehensive evaluation including CPET and body mass densitometry measurements. Additional information such as demographic variables were recorded. Subjects were enrolled in the study per institutional review board approved protocol.

Patients were grouped into three groups: those who achieved the peak exercise criteria, those with submaximal tests, and those whose tests had abnormal findings. Peak exercise tests were considered to be achieved if peak heart rate (HR) was $> 90\%$ predicted and the respiratory exchange ratio (RER) was > 1.1. We defined comorbidities as co-existent diabetes, hypertension, asthma, obstructive sleep apnea, or other cardiopulmonary disease. Patient's tests were considered abnormal if resting HRs were 120 beats per minute or greater (possibly reflecting undiagnosed heart disease), or if end tidal CO_2 after exercising was 50 mmHg or greater (likely reflecting hypoventilation syndrome). Tests were excluded if terminated prematurely due to machine malfunction or if bioelectrical impedance analysis (BIA) was not recorded.

Study procedures

Cardiopulmonary exercise stress testing (CPET)

Exercise testing was performed in the Exercise Laboratory at CUIMC in accordance with the American Thoracic Society guidelines(8,13) and performed using a standard Bruce protocol. Participants breathed through a mouthpiece, and expired gas volumes and concentrations were continuously analyzed using a computerized breath-by-breath exercise system (Vyaire Vmax 22c Loma Linda, CA). Minute ventilation (VE), volume of oxygen consumption (VO_2), carbon dioxide production (VCO_2), respiratory exchange ratio (RER=VCO_2/VO_2), and ventilatory equivalents for oxygen (VE/VO_2), and carbon dioxide (VE/VCO_2) were calculated on a breath-by-breath basis. HR and oxygen saturation were continuously monitored by 12-lead electrocardiogram (Cardio Soft, GE medical) and pulse oximetry (Maximo Radical 7). Effort is considered to be peak if HR achieved $>90\%$ of the predicted value and the peak RER at peak exercise was [?] 1.1. The peak VO_2 was recorded as the highest 20 second average of the final breath-by-breath data achieved during exercise. HR at VO_2 peak (pVO_2) and O_2 pulse (pVO_2 /HR at pVO_2) were also recorded.

Bioelectrical Impedance Analysis

BIA was used to calculate LBW and body fat percentage for all patients seen at the CABS Center at CUIMC using a Tanita Body Composition Analyzer, Model TBF-310, Tanita Corporation, Tokyo, Japan. This data was be collected and used for calculation of ideal body weight and development of regression equations.

STATISTICAL ANALYSIS

Conventional reference equations from healthy children on cycle ergometer(1) were employed using LBW and TBW. Spearman correlation was used to examine the correlation of the data between predicted and actual VO_2/kg, and intra-class correlation coefficient (ICC) was used to assess the agreement between measured and calculated peak VO_2.

Simple linear regression equations were calculated to predict pVO_2 for children with obesity as a function

of TBW in males and females separately. These equations were derived for the total group of peak exercise CPET studies, and also, for the subgroup of patients with comorbidities. These equations were calculated both for pVO_2 (mL/min) and pVO_2/kg (mL/kg/min).

Submaximal tests were not included in the regression analysis but rather the regression equations were applied to assess their functional capacity (by comparing their peak VO_2 as a percent predicted of the calculated reference values).

Results

During the specified timeframe, there were a total of 446 children and adolescents with obesity who underwent comprehensive bariatric surgery evaluation, of which 366 patients had a recorded BIA in their medical charts and underwent a CPET test without any equipment malfunction. Of these children and adolescents, 107 participants (29%) achieved peak exercise criteria and 240 completed tests were submaximal and 19 were abnormal. Patient categorization is summarized in Figure 1. Patient demographics and anthropometrics are described in Table 1. The participants' mean weight was 127 ± 21 kg, body fat 49.7 ± 6.8%, and LBW 63 ± 10 kg (Table 2). Among males in the peak group, lean muscle mass was 137.0 ± 26.5% of predicted(14) per age and among females in the peak group, lean muscle mass was 166.9 ± 20.9% of predicted(14) per age.

The mean exercise study time of males in the peak group was 7.07 ± 1.16 minutes. Males in the peak group performed for 56.2 ± 9.3% of the predicted time per age.(15) The mean exercise study time of females in the peak group was 6.51 ± 1.24 minutes. Females in the peak group performed for 64.9 ± 12.4% of the predicted time per age.

Among the peak studies, the mean pVO_2/kg was 22.2 ± 3.2 mL/kg/min (normal mean reference values: 40-49 mL/kg/min) when using absolute body weight. The mean pVO_2/kg using LBW was 44.8 ± 8.7 mL/kg/min. Using a conventional reference from healthy children on cycle ergometer(1), TBW estimated VO_2/kg to be 50.7 ± 7.0 % predicted, while LBW estimated it at 102.3 ± 17.6 % predicted as shown in Figure 2. Spearman correlation between measured pVO_2 and calculated peak VO_2 was 0.750 (0.476 for males, 0.604 for females) in the peak group ($p<0.01$), showing significant correlation, but the agreements were poor. (Intra-class correlation coefficient (ICC)=0.41, 95%CI 0.265-0.532).

Simple linear regression of pVO_2 on TBW in the peak group identified the following new equations for our population (*Equations 1-4*), with standard errors and R^2values summarized in Table 3:

Predicted peak VO_2(absolute, in mL/min) as a function of TBW (kg) in all males in the peak population:

pVO_2(mL/min) = 1571.6 + 12.2 * TBW(kg) + error (*Equation 1*), 95% CI (4.8, 19.7)

Predicted peak VO2 (absolute, in mL) as a function of TBW (kg) in all females in the peak population:

pVO_2(mL/min) = 1301.8 + 10.6 * TBW(kg) + error, (*Equation 2*), 95% CI (7.1, 14.1)

Predicted peak VO_2 (relative, in mL/kg/min) as a function of TBW (kg) in all males in the peak population:

pVO_2(mL/kg/min) = 34.06 - 0.074 * TBW(kg) + error, (*Equation 3*), 95% CI (-0.13, -0.018)

Predicted peak VO_2 (relative, in mL/kg) as a function of TBW (kg) in all females in the peak population:

pVO_2(mL/kg/min) = 31.76 - 0.084 * TBW(kg) + error, (*Equation 4*) , 95% CI (-0.11, -0.055)

Simple linear regression of pVO2/kg distribution in the peak group identified the following new equations for our population without comorbidities (*Equations 5-8*), with standard errors and R^2 values summarized in Table 3:

Predicted peak VO_2(absolute, in mL/min) as a function of TBW (kg) in males without comorbidities in the peak population:

pVO_2(mL/min) = 1380.8 + 13.9 * TBW(kg) + error, (*Equation 5*), 95% CI (4.1, 23.8)

Predicted peak VO2 (absolute, in mL) as a function of TBW (kg) in females without comorbidities in the peak population:

pVO_2(mL/min) = 1463.8 + 9.77 * TBW(kg) + error, (*Equation 6*), 95% CI (5.2, 14.3)

Predicted peak VO_2(relative, in mL/kg) as a function of TBW (kg) in males without comorbidities in the peak population:

pVO_2(mL/kg/min) = 33.33 - 0.066 * TBW(kg) + error, (*Equation 7*), 95% CI (-0.14, 0.0062)

Predicted peak VO2 (relative, in mL/kg) as a function of TBW (kg) in females without comorbidities in the peak population:

pVO_2(mL/kg/min) = 33.76 - 0.096 * TBW(kg) + error, (*Equation 8*), 95% CI (-0.13, -0.059)

The predicted peak absolute VO_2 (in mL/min) as a function of TBW (kg) is described for males (*Equation 9)* and females (*Equation 10)* with comorbidities included as an additional covariant. The predicted peak relative VO_2(in mL/kg/min) as a function of TBW (kg) is described for males (*Equation 11)* and females (*Equation 12)* . Descriptive statistics for *Equations 9-12* are summarized in Appendix Table 1. For Equations 9-11, comorbidities were not significantly associated with predicted peak VO_2 after adjusting for weight in each population. For *Equation 12* , the coefficient estimate for comorbidities is -1.12 (standard error: 0.56) with p-value 0.0485, which indicates that comorbidities are significantly associated with predicted pVO_2 (absolute, in mL/kg/min) at 5% significance level, after adjusting for weight in the female peak population. For all*Equations 9-12* , comorbidities did not interact in the relationship between weight and absolute or relative predicted peak VO_2.

pVO_2(mL/min) = 1619.1 + 12.22 * TBW(kg) -75.3 * comorbidities + error (*Equation 9)*

pVO_2(mL/min) = 1356.3 + 10.65 * TBW(kg) – 121.5 * comorbidities + error (*Equation 10)*

pVO_2(mL/kg/min) = 34.4 - 0.074 * TBW(kg) -0.55 * comorbidities + error (*Equation 11)*

pVO_2(mL/kg/min) = 32.3 - 0.083 * TBW(kg) – 1.12 * comorbidities + error (*Equation 12)*

We subsequently applied these equations to the submaximal patients without underlying cardiopulmonary disease. Demographics, anthropometric characteristics and CPET results are summarized in Appendix Table 2. Among the submaximal studies, the mean cardiopulmonary fitness (pVO_2/kg) was 20.5 ± 4.0 mL/kg/min when using absolute body weight. The mean pVO_2/kg using LBW was 33.6 ± 10.9 mL/kg/min. Using a conventional reference from healthy children on cycle ergometer, TBW estimated pVO_2/kg to be 46.6 ± 8.5 % predicted, while LBW estimated it at 76.1 ± 23.6 % predicted. Using TBW, a conventional reference from healthy children, the estimated pVO_2 to was 44.1 ± 3.4 % predicted, while the present study's new equations (*Equations 1 and 2)* estimated it at 93.5 ± 16.3 % predicted.

Figure 3 depicts HR vs. relative pVO_2 using TBW (A) and HR vs. relative VO_2 using LBW (B) at each stage of exercise throughout the Bruce protocol (Rest, Stage 1, Stage 2, Stage 3, Stage 4) with predicted normal (from up to down: upper limit, mean, lower limit) shown for comparison (pVO_2 truncated at 50). A normalization of HR response is seen when LBW is used.

Discussion

In this retrospective study, we established normative CPET treadmill data for children with obesity. We used BIA to calculate patients' LBWs and showed an improved method of predicting their peak oxygen consumption compared to traditional use of TBW. We also developed normal reference regression equations for children and adolescents with obesity and applied our new equations to our larger cohort.

Our first aim was to study the use of LBW to predict pVO_2 within this population. Within children and adolescents, some have shown that those with obesity have a larger amount of LBW and are often stronger than youth their same height, given that their muscles are accustomed to carrying the extra load attributed by their fat mass.(16,17) Our work confirmed this finding, with our participants having 137% and 167%

predicted lean muscle mass in males and females, respectively, indicating hypertrophied muscle in the setting of increased workload rather than an atrophied group of muscles which may have been anticipated in a deconditioned group. Several studies have shown that fat free mass alone can be used to predict pVO_2, suggesting that these children do not have impaired cardiopulmonary system when theirs studies are corrected appropriately for their LBW.(18–22) Other work, however, has suggested that while not metabolically-active, fat mass has a sex- and age-dependent effect on pVO_2 as children enter puberty and adolescence,(11) or that normalizing predicted $pVO_2$to LBW in this population is not mathematically appropriate.(23) In children both with and without obesity, the concept of ideal body mass has aided in assessing CRF in children and adolescents, given children's evolving body composition during puberty and physiologic responses that vary into adulthood.(16,24) In our peak group adolescents, we also found that LBW showed greatly improved ability to predict an accurate maximum pVO_2 (102.3 ± 17.6 % versus 50.7 ± 7.0 % predicted) as displayed in Figure 2. Further, we showed that the use of LBW normalizes the HR response when depicting HR versus relative VO_2(Figure 3) such that the data fall within the predicted distribution.

While previous studies have evaluated the use of LBW to predict pVO_2 in pediatric patients with obesity, these studies have only been conducted in cycle-ergometer based tests rather than on a treadmill.(11,18,25,26) In our population of patients with obesity, many are unable to use a cycle-ergometer given device weight limits, hence necessitating a need for equations for treadmill-based studies. Multiples methods for calculating LBW exist. In pharmacology, the traditionally-used method for dosing patients with obesity is the ideal body weight equation, a surrogate for LBW, called the Devine equation.(27,28) However, given that the Devine equation(27) is applicable for patients who are at least 5 feet tall, there is no consensus for smaller patients (i.e. children) on a validated tool to calculate ideal body weight, leading experts to suggest bioelectric impedance or alternative methods to calculate ideal body mass in children with obesity.(29) Bioelectric impedance has been shown to be inexpensive and highly reproducible,(30) and uses the known electrical properties of biologic studies and a scale to estimate a patient's fat free body mass.(31) Multiple skin fold anthropometry is also commonly employed to calculate lean body mass in nutritional science and some exercise studies,(20,22) however this method risks errors such as inter- and intra-examiner reproducibility, and the compressibility of subcutaneous fat and calibration of skinfold calipers.(30,32) Alternatively, others have studied CPET normalization using Dual X-ray absorptiometry(11,18,19,23) to allow for normalization of peak VO_2 to LBW, but this method is uncomfortable, expensive and exposes patients to radiation making it a difficult method for large-scale use. Although many different modalities of calculating LBW exist, our work only evaluated the use of BIA. Given its affordability and accuracy, we suggest that CPET laboratories consider its use to derive LBW, which can better predict VO_2 and help normalize VO_2 interpretations in CPET study analyses.

Next, given that BIA is not always available, we devised predictive reference equations for patients with obesity using our peak subgroup because previous equations under-predict and under-report these patients' functional capacity. Compared to a conventional reference from healthy children, our new equations for absolute pVO_2(*Equations 1 and 2)* were much more accurate at predicting absolute peak VO_2, which suggests that our equations be used as standard to predict pVO_2 in the adolescent population with obesity. Further, we found in that in both sexes, relative pVO_2 was not significantly impacted by the use of comorbidities as a coefficient in these equations. These findings shows that our equations for absolute pVO_2(*Equations 1 and 2)* in males and females, respectively, may be used as predictive equations in the adolescent population with obesity regardless of comorbidities.

Our study is novel and impactful in that it has clearly demonstrated the fallacies associated with interpretation of CPET studies in children and adolescents with obesity when using weight adjusted VO_2values, given the changes noted in percent predicted values when using LBW rather than TBW. The generation of age-specific reference equations for pediatric patients with obesity performing CPET on the treadmill can be applied to larger patient populations. Our reference equations were internally validated by applying them to the CPET studies that were submaximal at our institution and a similar trend of accuracy was noted. Our future directions include prospectively applying these new reference equations to all routinely performed CPET studies among patients with obesity. In the absence of LBW measurements, these new

reference equations can be a useful substitute for estimation of predicted values.

Limitations

Our study is not without limitations. Firstly, the study is limited by its retrospective nature of data collection based on chart review. In our project, we assumed that 19- to 20-year-old patients in our population had the same predicted LBW(14) as those aged 18 years old in the healthy population as a study covering all age ranges could not be identified in the literature. In our study, we also assumed that 18- to 20-year-old patients in our population had the same expected exercise times(15) as those aged 15- to 17 years old in the healthy population as a study covering all age ranges could not be identified in the literature.

Conclusions

Similar to adults, when pVO_2 is corrected for LBW rather than per kilogram weight, children and teenagers with obesity demonstrate normal oxygen consumption. A novel set of equations can be used to pVO_2 in the adolescent population with obesity when BIA or other methods of calculating LBW are not available.

Conflicts of Interest

None of the authors have any conflicts of interest to disclose.

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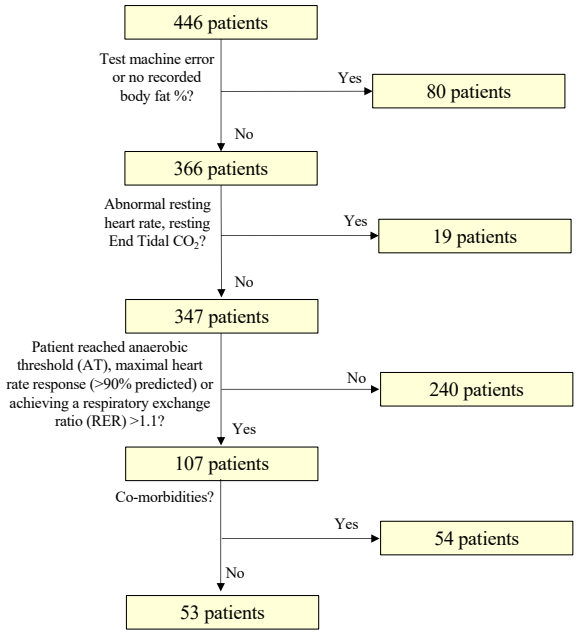

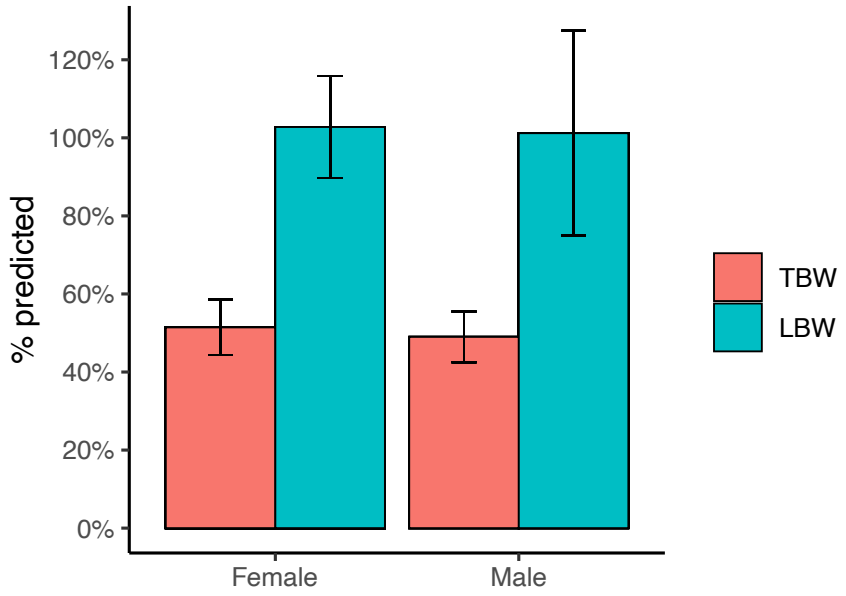

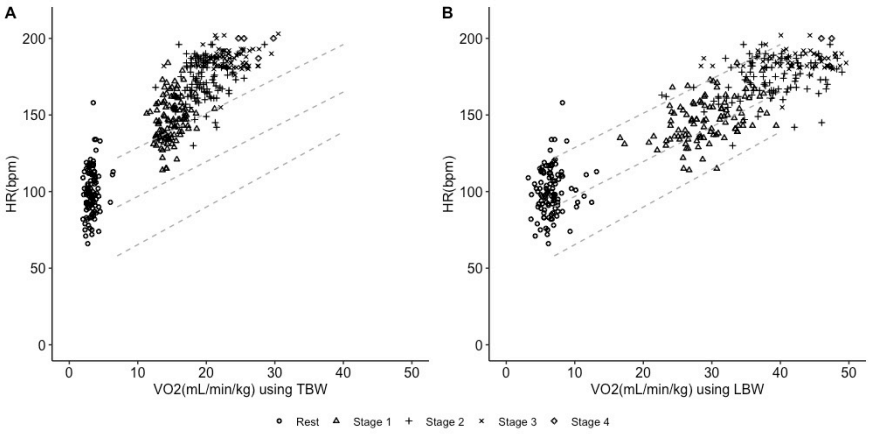

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