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Original Article

Developing First Native Regression Equations to Predict of Cardiorespiratory Fitness in Healthy Boys

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Abstract

Background: Cardio-respiratory fitness (CRF) is a strong predictor of overall health and is considered a key physiological measure in health care settings. Maximal oxygen uptake (VO_{2max}) is considered the gold standard for measuring CRF. Non-exercise VO_{2max} regression equations provide a safe, simple and relatively accurate means of measuring CRF in the general population. This study aimed to develop first native regression equations to predict of CRF without exercise test in Iranian healthy boys.

Methods: Laboratory gold standard CRF and anthropometric variables were measured in 597 healthy boys (8-17 yr) in Hmadan City, Iran in 2019. Multiple regression analysis was used to generate CRF regression equations. Cross validation of the CRF regression equations was assessed using PRESS statistics, Pearson correlation, Bland-Althman plot and paired t-test.

Results: CRF regression equations based on age, body mass index, body fat and resting heart rate were developed (R^2=0.602 – 0.639, SEE = 3.42 – 3.73 ml/kg/min). PRESS statistics show that, shrinkage of the R^2 (0.04 – 0.06) and the increment of SEE (0.18 – 0.25 ml/kg/min) is minor. There was strong correlation (R =0.847–0.883, P<0.001) and no significant difference (min diff= 0.09–0.18 ml/kg/min, P>0.05) between measured and predicted CRF. The Bland-Altman plot illustrates the strong agreement between the two values.

Conclusion: We introduced simple and satisfactorily accurate CRF regression equations based in healthy boys. Prediction of CRF of the boys by regression equations would provide a simple tool for assessing cardiorespiratory fitness in large studies including Iranian boys.

Keywords: Cardiorespiratory fitness; CRF regression equations; Boys; Public health

Introduction

Cardiorespiratory fitness (CRF) is an important indicator of health which is measured in research, exercise, and health-related settings (1). The assessment of CRF is valuable when educating individuals about their overall fitness status, developing exercise programs and stratifying cardiovascular risk (2). However, CRF assessment is rarely evaluated in many healthcare settings and large-scale studies.

Maximal oxygen uptake (VO_{2max}), measured during a maximal graded exercise test (GXT), is considered the gold standard for measuring CRF. Nevertheless, this approach often is not practical because it requires expensive and sophisticated equipment, qualified examiners, and long duration of testing sessions (3). Because of these drawbacks, other methods with less complexity have been developed to determine VO_{2max}. These methods use either field exercise tests (4, 5) or non-exercise tests to predict VO_{2max} (6-8). Nevertheless, prediction of VO_{2max} by field exercise test is impossible in large scale and epidemiological studies, where gathering the health and physical fitness related information in short time is essential (9, 10).

To overcome these difficulties, researchers have developed the non-exercise (N-EX) models to predict CRF. Studies confirmed that measurement of CRF from N-EX models is practical and viable when exercise testing is not feasible (9, 11). Previous studies show N-EX VO_{2max} equations are relatively accurate, quick and easy way to predict the CRF (9, 10). N-EX equations utilizes predictive variables such as gender, age, height, weight, body mass index (BMI), body fat percentage (BF%), resting heart rate (RHR) and quantity of physical activity (PA) for predicting the VO_{2max} (2, 6-8, 10, 12-18).

N-EX VO_{2max} equations may not be accurate in other nations because of the inherent differences in ethnic, body composition and PA habits (9). Several N-EX VO_{2max} equations have been developed in adults (2, 14-17). To date, a few studies have developed N-EX VO_{2max} equations in healthy girls and boys, but have small samples sizes (n=22-100) (6, 7, 13). Therefore, we aimed to develop and cross-validate N-EX VO_{2max} regression equations in healthy Iranian boys.

Methods

Participants

The present investigation consisted of healthy boys (n=597 boys; age: 12.33±2.75 yr; height: 153.75±15.78 cm; body mass: 47.71±17.60 kg; body mass index: 19.55±4.23 kg m2; body fat: 23.29±10.14%) volunteered for the study in 2019 (Table 1). We divided participants in Prediction (n=349) and Validation (n=248) groups by random order. Healthy boys were recruited from schools. None of the participants had background of cardiovascular, respiratory, neuromuscular, anatomical, and metabolic abnormalities and long-term medications. Also, current sample does not include athletes.

Table 1: Characteristic (Mean±SD) of participants (n=597)

Variable	*Total (n=597)*	*Min*	*Max*
Age (yr)	12.33±2.75	7.42	17.58
Height (cm)	153.75±15.78	120	193.5
Weight (kg)	47.71±17.60	20.5	113
BMI (kg/m²)	19.55±4.23	11.69	35.27
BMI percent (%)	57.66±21.25	2.10	99.83
BF (%)	23.29±10.14	8.38	64.97
RHR (bpm)	82.69±9.66	58	108
VO_{2max} (ml/kg/min)	41.24±6.00	22.10	54.80
RER	1.21±0.07	1.01	1.50
HR_{max} (bpm)	202.4±6.3	190	222
HR_{max} (%)	101.5	94.94	112.33

BMI: Body Mass Index, BF (%): Body Fat Percentage, RHR: Resting Heart Rate, VO_2max: Maximum Oxygen Uptake, RER: Respiratory Exchange Ratio, HRmax: Measured Maximal Heart Rate, HRmax (%): Percent of the Theoretical Maximal Predicted HR

The research project was approved by the Ethical Committee of Medical Science University of Hamadan (UMSHA.REC.1394.116). It has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Written consents were taken from the parents of the boys.

Demographic and Anthropometric measurements

The exact age was calculated from the date of measurement by the date of birth (0.1 years). Body mass (0.1 kg), height and seated height (0.1 cm) were measured with a stadiometer (Dig ital Free-Standing Stadiometer BSM170; Inbody, Seoul, Korea). BMI was calculated by dividing the body mass in kilograms by the square of height in meters (kg $.m^{-2}$). Moreover, BMI Percentile was determined according to the Centers of Disease Control and Prevention (CDC) growth charts. BF% was assessed by skinfold thickness based on Slaughter equation (19). Skinfold thicknesses were measured on the left side of the body to the nearest 0.1 mm with a skinfold calliper (Lange Skinfold Caliper - C-130, UK), at the triceps and subscapular sites. The mean from three separate measurements of skinfold thicknesses was used. RHR was measured by telemetry (Heart Rate Transmitter Model T34; Kempele, Finland) after the boys were seated for 10 min.

Maximal GXT

VO_{2max} was measured with a maximal GXT according to the modified Bruce protocol (3) with a treadmill (Saturn 300/125; h/p/cosmos, Nussdorf-Traunstein, Germany) in the exercise physiology laboratory at 19-21°C, relative humidity 39%-43% at 1860 m above sea level. Breath-by-breath gas samples were collected via a face-mask (Hans Rudolph, Kansas City, Missouri) and were analyzed throughout the test by open-circuit calorimetry via ergospirometry (PowerCube; Ganshorn Medizin Electronic GmbH, Niederlauer, Germany). Exercise heart rate was monitored during the GXT by telemetry (Heart Rate Transmitter Mo del T34; Kempele, Finland). The boys were asked to avoid heavy physical activities 24 hours before the GXT. VO_{2max} was calculated as the greatest mean breath-by-breath VO2 during 20 consecutive seconds. To confirm that boys attained their VO_{2max}, at least 2 of the 3 following criteria were met: respiratory exchange ratio (RER) >1.10, (2) maximal HR was no less than 90% of the age-predicted maximal HR (208–0.7 × age) (20), and (3) the subject was exhausted and unable to continue despite verbal encouragement (3). In present study, all the boys attained VO_{2max} criteria (Table 1).

Statistical analysis

Pearson's product correlations were calculated between measured VO_{2max} and independent variables (age, weight, BMI, BF%, and RHR). Stepwise multiple regression analysis was used to generate N-EX prediction equations for VO_{2max}. The goodness of fit and precision of the regression equations were evaluated using multiple coefficient of determination (R^2), absolute standard error of estimate (SEE), partial SEE (SEE%), normality of errors and non-correlation of errors (Durbin Watson test) (21). Besides, collinearity of N-EX VO_{2max} equations was controlled by Variance inflation factor and Tolerance indices (22).

For cross-validation purpose, predicted residual sum of squares (PRESS) statistics (23) were computed to estimate the degree of shrinkage one could expect when the VO_{2max} prediction equation is used across similar, but independent, samples. Measured and predicted VO_{2max} values were compared using paired student's t test, the Bland-Altman plot and Pearson's product correlation in validation samples (n=248).

We used the rule of 40 events per variable (EPV ≥ 40) to determine acceptable sample size (24). Based on study literature six predictive variables easily obtained (i.e., age, height, weight, BMI, BF% and RHR) were related to VO_{2max} (6, 7, 12) Therefore, the minimal sample size was 240 subjects to eliminate bias in regression coefficients. To increase the accuracy of the prediction models, we selected more subjects (n=349) in prediction group. All analyses were performed using SPSS software version 24, (IBM Corp., Armonk, NY, USA) and alpha level was set at $P<0.05$.

Results

Characteristics of study variables are presented in Table 1. Seventy one percent of the boys had normal weight, 22% of the boys had over weight and the rest had obese. All participants met the VO_{2max} criteria (i.e., RER=1.21±0.07 and maximal HR =202.4±6.3 bpm).

Correlations of independent variables with VO_{2max} were statistically significant except for height (P<0.01) and ranged from a low of 0.105 for age to a high of -0.747 for BF (Table 2). The results of the multiple regression analyses are presented in Table 3.

Table 2: Correlation matrix of study variables (n=597)

Variable	*VO_{2max}*	*Age*	*Height*	*Weight*	*BMI*	*BF*	*RHR*
VO_{2max} (ml/kg/min)	__						
Age (years)	0.105$^{\infty}$	__					
Height (cm)	0.006	0.895*	__				
Weight (kg)	-0.384*	0.747*	0.831**	__			
BMI (kg/m²)	-0.639*	0.451*	0.498**	0.884*	__		
BF (%)	-0.747*	0.173*	0236	0.625*	0.833*	__	
RHR (bpm)	-0.314*	-0.363*	-0.294*	-0.191*	-0.035	0.154*	__

VO_{2max}: maximum oxygen uptake, BMI: Body mass index, BF%: body fat percentage, RHR: resting heart rate. $^{\infty}P$<0.05, $^{*}P$<0.01

Table 3: Non-exercise VO_{2max} regression equation in prediction group (n=349)

Prediction model	*Coefficients*	*R^2*	*SEE (ml/kg/min)*	*SEE%*	*R^2p*	*SEEp (ml/kg/min)*
Model 1*		0.602	3.73	9.04%	0.54	3.98
Constant	51.605					
Age (y)	1.057					
BMI (kg/m²)	-1.199					
Model 2*		0.634	3.58	8.68%	0.59	3.77
Constant	62.914					
Age (y)	0.875					
BMI (kg/m²)	-1.156					
RHR (bpm)	-0.12					
Model 3*		0.614	3.67	8.9%	0.57	3.89
Constant	45.487					
Age (y)	0.518					
BF (%)	-0.458					
Model 4*		0.639	3.42	8.75%	0.60	3.60
Constant	52.972					
Age (y)	0.407					
BF (%)	-0.442					
RHR (bpm)	-0.079					

VO_2max: maximum oxygen uptake, BMI: Body mass index, BF%: body fat percentage, RHR: resting heart rate, SEE: Standard error of the estimation, SEE% = SEE/mean of measured value × 100 as partial SEE, R^2: coefficient of determination, SEEp, PRESS standard error of estimate, R^2p, PRESS multiple correlation coefficients. $^{*}P$<0.01

We introduced four N-EX VO_{2max} equations. Based on our results age, BMI, BF and RHR explained 60.2 to 63.9% of the VO_{2max} variance of the boys (8-17 yr) according to the following equations:

Equ 1 VO_{2max} (ml/kg/min) = 51.605 + (1.057 × age) - (1.199 × BMI kg/m^2)

(R^2 = 0.602 and SEE= 3.73 ml/kg/min ~ 9.04% measured VO_{2max}).

Equ 2 VO_{2max} (ml/kg/min) = 62.914 + (0.875 × age) - (1.156 × BMI kg/m^2) – (0.12 × RHR_{bpm})

(R^2 = 0.634 and SEE= 3.58 ml/kg/min ~ 8.68% measured VO_{2max}).

Equ 3 VO_{2max} (ml/kg/min) = 45.487 + (0.518 × age) - (0.458 × $BF_{\%}$)

(R^2 = 0.614 and SEE= 3.67 ml/kg/min ~ 8.9% measured VO_{2max}).

Equ 4 VO_{2max} (ml/kg/min) = 52.972 + (0.407 × age) - (0.442 × $BF_{\%}$) – (0.079 × RHR_{bpm})

(R^2 = 0.639 and SEE= 3.42 ml/kg/min ~ 8.75% measured VO_{2max}).

The K-S normality test demonstrated that the errors are distributed normally. Durbin Watson statistic showed no problems with serial autocorrelation (D-W =1.765 – 1.862). Also, Variance inflation factor and Tolerance indices showed no noticeable collinearity of N-EX VO_{2max} equations. The cross-validation PRESS statistics of the N-EX VO_{2max} equations showed minimal shrinkage in predictive accuracy. As, shrinkage of the R^2 (0.04 – 0.06) and the increment of SEE (0.18 – 0.25 ml/kg/min) for the N-EX VO_{2max} equations was minor (Table 3). There was strong correlation between measured and predicted VO_{2max} (R =0847 – 0.883, P<0.001) and no significant difference between measured and predicted VO_{2max} in Validation group (min diff= 0.09 – 0.18 ml/kg/min, ~ 0.21 – 0.42% measured VO_2max, P>0.05) (Table 4). The Bland-Altman plot illustrates the strong agreement between the measured and predicted VO_{2max} values in our proposed N-EX VO_{2max} equations (Fig. 1: A, B, C and D). But, Predicted VO_{2max} based on two foreign equations were significantly different from measured VO_{2max} (min diff= -6.37 to - 6.97 ml/kg/min, ~ 14.82 – 16.17% measured VO_2max) (Table 4 and Fig. 2: A and B).

Table 4: Comparison our proposed N-EX VO_{2max} equations and previous studies with measured VO_2max in Validation group(n=248)

N-EX VO_{2max} equations	*measured (ml/kg/min)*	*predicted (ml/kg/min)*	*Mean diff (ml/kg/min)€*	*Mean diff (%)*	*R*
	42.96±5.86	------	------	------	------
1	------	42.80±5.48	0.18±3.16	0.42	0.847*
2	------	42.79±5.45	0.15±2.96	0.35	0.870*
3	------	43.10±5.13	0.16±3.10	0.37	0.859*
4	------	42.94±5.14	0.09±2.91	0.21	0.883*
Bonen	------	49.92±5.02	-6.95±3.88*	16.17	0.757*
Erdman	------	49.33±6.69	-6.37±3.63*	14.82	0.841*

€ Mean diff: Measured – Predicted VO_{2max}, Mean diff %: (Mean diff / Measured VO_{2max}) ×100, ¥: R: Correlation between Measured and predicted VO_2max, *P<0.001

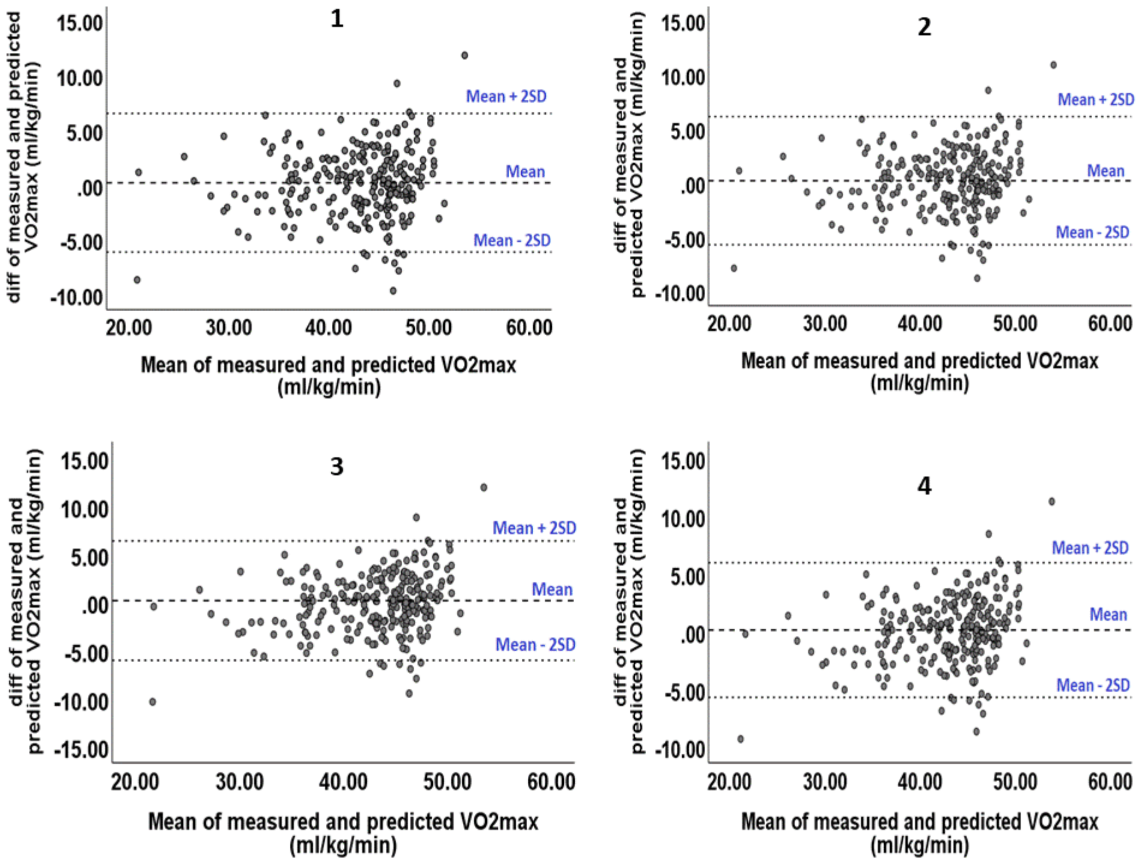

Fig. 1: Bland Altman plot for estimated and measured VO_{2max} (ml/kg/min) in the Validation group (n=248) by our proposed N-EX equations (1-4). Dashed line mean difference. Dotted line: mean diff ±2SD

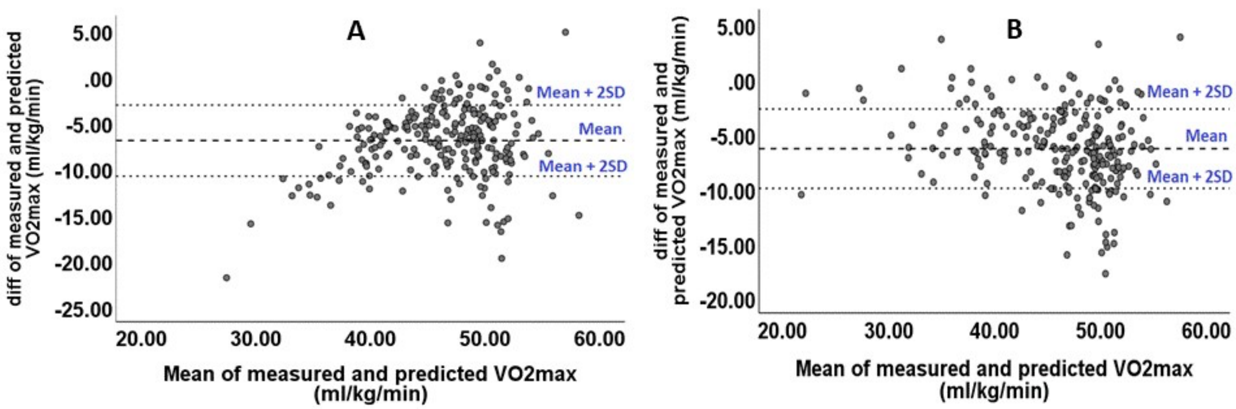

Fig. 2: Bland Altman plot for estimated and measured VO_{2max} (ml/kg/min1) in the Validation group (n=248) by foreign N-EX equations (A: Bonen & B: Erdman). Dashed line mean difference. Dotted line: mean diff ±2SD

Discussion

The results of the present study introduced satisfactory N-EX VO_{2max} equations using age, BMI, BF% and RHR in healthy boys (R^2= 0.602 – 0.639, SEE = 3.42 – 3.73 ml/kg/min, P<0.001). Our proposed N-EX VO_{2max} equations more feasible for evaluation of youth CRF in health-related setting and epidemiological studies.

CRF reflects the overall efficiency of the cardiovascular system in all ages. The decision to measure of CRF in most settings is influenced by the feasibility and cost of equipment (9, 25). Despite the limitations of equations, application of CRF from non-exercise methods showed accuracy and predictive ability (9). Because N-EX predictor variables are easily measured, experts of health, exercise science, preventive medicine, clinical exercise testing and epidemiology have suggested that the estimation of CRF from N-EX VO_{2max} equations would be most appropriate for widespread use in health related settings if they have sufficient validity (17, 19).

The independent variables used in this study were related with measured VO_{2max} except for height (Table 2). This result was also observed in previous studies on children and adolescents in which the higher the BMI and/or BF%, the lower the VO_{2max} (26-28). To date, N-EX VO_{2max} predictor variables include age, gender, weight, BMI, BF% and RHR. A number of studies have documented the correlation between anthropometric variables with VO_{2max} in healthy girls and boys (6, 7, 12, 13) and adults (2, 8, 10, 14-18). Consistent with our results, weight, BMI, BF and RHR have been cited as the most important variables affecting VO_{2max} (6, 7, 12). These findings document the value of using anthropometrics implemented easily, when evaluating CRF in clinical fields and large epidemiological cohorts.

The adaptive responses of the cardiovascular system to regular PA appear to include a reduction in sympathetic activity and an increase in parasympathetic activity during rest and at different absolute intensities of exercise (29). High VO_{2max} is associated with a low RHR. These results illustrate the significant relationship between VO_{2max} and vagal tone in control of RHR. Individuals with a higher VO_{2max} maintain lower resting heart rates mainly via an increase in parasympathetic tone (30). Therefore, the use of RHR variable can be a good alternative to PA variable in N-EX VO_{2max} equations. In the present study, significant relationship (R= - 0.314) was observed between VO_{2max} and HRR (Table 2).

To our knowledge, a few attempts have been conducted to develop N-EX VO_{2max} equations in healthy boys (6, 7, 12, 13). In present study we developed four N-EX VO_{2max} equations based on anthropometric and physiologic variables in healthy boys (R^2= 0.602 – 0.639, SEE = 3.42 – 3.73 ml/kg/min, P<0.001). In our proposed native N-EX VO_{2max} equations, age, BMI, BF% and RHR could explain approximately 60% to 64% of the VO_{2max} variance of healthy boys with percent error of 8.75% to 9.04%.

Compared to our study, Erdmann et al developed N-EX VO_{2max} equations in 11-14 yr boys (n=83) in the United States. According to their study, VO_2max could be estimated by BMI, body fat percent and PA (R= 0.69-0.82, SEE= 4.46-5.58 mL/kg/min) (7). In study of Bonen and colleagues VO_2max of the boys (7-15 year, n=100) could be predicted by age, height and weight (R= 0.52, SEE= 4.4 mL/kg/min) (6). Dencker et al developed N-EX VO_2max equations in children age 6-to 7-yr-old (n = 436) in Denmark (12). According to their study, fat free mass, body fat, sex and PA explained 62% of relative VO_{2max} of the children. Shephard and colleagues developed N-EX VO_2max equations by anthropometric and body strength indices in healthy girl and boys of Canada (9-13 year, n = 45) (13). Differences in samples, age range, health status, type, number of predictor variables and differences in the ethnicity may explain the range of R and SEE values of previous N-EX VO_{2max} equations.

To ensure the performance of the proposed N-EX VO_{2max} equations, we conducted a cross-validation analysis based on PRESS statistics in Prediction group (n=349) (23). Our results showed that shrinkage of the R^2 (0.04 – 0.06) and the increment of SEE (0.18 – 0.25 ml/kg/min) for N-EX VO_{2max} equations were minor (Table 3), supporting the validity of the proposed N-EX VO_{2max} equations in the current study. Furthermore, the high correlations between measured and predicted VO_{2max} values (R =0847 – 0.883, P<0.001) (Table 4) and good agreement between two measures (Fig. 1: A to D) in the Validation group (n=248) supports the performance of the proposed N-EX VO_{2max} equations in healthy boys. Moreover, when multiple predictors are used in regression models, the validity of models is improved (31). Therefore, in our proposed N-EX VO_{2max} equation two or three predictive variables (i.e., age BMI, BF% and RHR) improved the N-EX VO_{2max} equations.

In the present study we compared foreign N-EX VO_{2max} equations (6, 7) with measured VO_{2max}. Predicted VO_{2max} based on two foreign equations were significantly different from measured VO_{2max} (mean difference = -6.37 to 6.95 ml/kg/min, $P<.001$) (Table 4). In the other words, these N-EX equations significantly over estimate (min diff= -6.37 to -6.97 ml/kg/min, ~ 14.82–16.17% measured VO_{2max}) the VO_{2max} of the boys of our study. This bias in prediction of VO_{2max} because of the inherent differences in ethnic, age ranged, body composition and PA habits.

In present study, we used a relative scale of VO_{2max} (ml/kg/min). However, in some studies, absolute scale of VO_{2max} (L/min) was used in boys (6, 13). In boys because of changes due to growth process, relative scale of VO_{2max} (ml/kg/min) is more sensitive than absolute scale VO_{2max} (L/min) and it provide accurate index of the CRF (32).

In this study, PA was not measured via questionnaire. They take a long time to complete. Besides, it may be individuals tend to overestimate their PA level (33). Furthermore, youth tend to misinterpret questionnaires which may lead to inaccuracy of PA levels (34). Dencker et al. reported in children that physical activity scores explained only an additional 4-7% in N-EX VO2max prediction equations (12). N-EX VO_{2max} prediction equations that use simple objective variables (e.g., age, weight, BMI, BF% and RHR) have utility in health-related epidemiological studies.

The large sample size (n=597), direct measurement of the VO_{2max} during the GXT by treadmill, wide age range and cross-validation of regression equations help support the generalizability of the N-EX VO_{2max} equations in healthy Iranian boys. Nevertheless, future studies are needed to evaluate the accuracy and generalizability of the proposed N-EX VO_{2max} prediction equations in a variety of samples. In addition, because the ease of measuring age, BMI, BF% and RHR, it is believed that utilization of N-EX VO_{2max} equations can be a routine component of CRF examination in health-related settings especially in epidemiological studies.

Limitations of present study need to be considered when using N-EX VO_{2max} equations. Our N-EX VO_{2max} equations may have limited generalizability because it was developed in a group of healthy Iranian boys. Moreover, we could not measure girls' data in this study. Therefore, the stability of the N-EX VO_{2max} equations is unknown in different groups (e.g., girls, adults, patients, and other racial groups).

Conclusion

We introduced simple and satisfactorily accurate N-EX VO_{2max} equations based on age, BMI, BF% and RHR in healthy Iranian boys (R^2=0.602–0.639, SEE = 3.42–3.73 ml/kg/min, $P<0.001$). Prediction of VO_{2max} based on simple N-EX variables would give an easy, inexpensive, safe and simple tool for assessing CRF in large studies including Iranian boys.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interest

The authors declare that there is no conflict of interest.

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