Original Article

Design and cross-validation of prediction equation based on 6-minute walk test for assessing the cardiorespiratory efficiency in Iranian adolescent boys

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Abstract

Background and aims: Measurement of the cardiorespiratory fitness (CRF) (VO2peak) is not possible in every clinical and exercise setting due to complexity, cost, and time required. Submaximal field exercise test in an alternative method. Among exercise tests, the 6-minute walk test (6MWT) measures the maximal distance which a person can walk in 6 minutes. The purpose of the present study was to develop and cross-validate the VO2peak prediction equation based on the 6MWT in boys.

Methods: VO2peak was measured by Bruce treadmill protocol with gas analysis in 157 healthy boys (13-17 years old). The 6MWT and anthropometric variables were measured according to standard methods. Data were analyzed using Kolmogorov-Smirnov test, Pearson correlation, and multiple regression analysis.

Results: It was found that VO2peak of the boys had a significant correlation with 6MWT and anthropometric variables (r=0.318-0.853). VO2peak of the adolescent boys could be predicted by the distance walked in 6 minutes and body mass index (BMI) (R^2 = 0.825, SEE = 2.81 mL/kg/min, $P<0.001$). When the new VO2peak prediction equation was applied for the subjects of this study, predicted VO2peak had a high correlation with measured VO2peak (r = 0.908, $P<0.001$).

Conclusion: The 6MWT and proposed native VO2peak prediction equation could be used as a simple and safe tool for measurement of the CRF in the boys. It seems that physicians, exercise and fitness coaches, and physiotherapists could be able to evaluate the effect of medical and exercise prescriptions on the CRF of the boys via performing the 6MWT. This claim needs future studies.

Keywords: Cardiorespiratory fitness; VO2peak prediction equation; Field exercise tests

Introduction

An individual's response to exercise test is an important health related assessment tool, since it provides the composite assessment of their respiratory, cardiac, and metabolic systems. Cardiorespiratory fitness (CRF) is an important health indicator which is measured in research, exercise, and health related settings (1). CRF reflects the functional capability of the heart, blood vessels, blood, lung, and relevant muscles during various types of exercise demands (2). Maximal oxygen uptake (VO2peak) or aerobic capacity which is measured during a maximal graded exercise test (GXT) is considered the golden standard of the CRF (2). Nevertheless, direct measurement of VO2peak is restricted due to lack of expensive and sophisticated equipment, qualified examiners, and long duration of testing sessions. Therefore, utilization of this method is impossible in every setting particularly in public spaces (such as physical education classes, gymnasiums), large scale research studies, and so on. (3). Hence, when the direct measurement of VO2peak is not feasible,

submaximal field exercise tests represent useful alternatives for estimating the VO2peak. Furthermore, VO2peak prediction equation could have practical implication in prescribing exercise training programs (1,2).

Submaximal field exercise tests provide feasible, safe, easy to administer, and inexpensive techniques for prediction of the aerobic capacity. In general, there are two common types of tests used for the estimation of VO2peak in the field setting: either a timed completion of a set distance or maximum distance for a set time (2). That is why the performance score obtained during field exercise test (time, distance, and exercise heart rate) could be a useful alternative to estimate the aerobic capacity (1,2).

Among the available varieties of exercise testing protocols for this purpose, the 6-minute walk test (6MWT) is an inexpensive, safe, and easily administered test with a functional ability (3). It is a self-based walking test which measures the maximum distance walked over a 6-minute period (4). There has been a substantial body of literature published looking at validity and reproducibility

of the 6MWT in healthy children and adolescents (5-11). Moreover, today, the 6MWT is a widely used tool for measuring the response to various rehabilitation interventions in cardiovascular and pulmonary diseases, due to its easy implementation and better acceptance (3,4).

Correlation between objectively measured VO2peak and 6MWT in the healthy children and adolescents has been reported in previous studies (R=0.44-0.723) (5,12). But no prediction of VO2peak from the 6MWT has been reported. To the best of our knowledge, only one study developed a model for predicting VO2peak from 6MWT in the obese youth, in which the aerobic capacity of the obese youth could be estimated by the distance walked in 6 minutes and body mass index (BMI) (13). Although the coefficient of determination (R^2) and standard error of estimate (SEE) for the regression equation were not cited.

Some studies have reported the application of the 6MWT for the estimation of VO2peak in healthy and sick subjects. In obese women, the aerobic capacity was adequately predicted by the 6MWD by a linear regression equation (14). In addition, the 6MWT was able to accurately predict the aerobic capacity in the children with pulmonary hypertension (15) and in the individuals with aneurysmal subarachnoid hemorrhage (16). Furthermore, the 6MWT (17) and 3-minute walk (18), combined with demographic variables provide a reasonable estimation of aerobic capacity in healthy adults (r^2= 0.60–0.72). To our knowledge, there is no study regarding the capability of the 6MWT for the estimation of aerobic capacity in the healthy children and adolescents in a relatively large sample size.

Therefore, the purpose of the present study was to develop and cross-validate the VO2peak prediction equation based on the 6MWT in boys.

Materials and Methods

Participants

This study included 157 healthy boys aged from 13 to 17 years old who were voluntarily recruited from schools in Hamedan, Iran. None of the participants had a history of cardiovascular, respiratory, neuromuscular, anatomical, and metabolic abnormalities or long-term medications that could affect the study variables. The research project was approved by the Ethics Committee of Hamedan University of Medical Sciences (IR.UMSHA.REC.1394.116) and was therefore performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Written informed consents were taken from the parents of the participants.

Demographic and anthropometric measurements

The exact age was calculated from the date of measurement by the date of birth (0.1 years). Body mass and height (0.1 cm) were measured using a stadiometer (Digital Free-Standing Stadiometer BSM170, Korea) to the nearest 0.1

kg and 0.1 cm respectively. To this end, boys were asked to wear light clothing and no shoes. BMI was calculated by dividing the body mass in kilograms by the square of height in meters ($kg.m^{-2}$) (2).

Maximal aerobic capacity

VO2peak was measured using a maximal GXT with treadmill (h/p/cosmos Saturn 300/125, Germany) according to the modified Bruce protocol (2) at the exercise physiology laboratory at temperature $19°C-21°C$, relative humidity 39%-43% at 1860 m above sea level. Breath-by-breath gas samples were collected using a comfortably fitted facemask (Hans Rudolph, Kansas City, MS, USA). The samples were then analyzed throughout the test by open-circuit calorimetry using the ergospirometry (PowerCube, Ganshorn Medizin Electronic GmbH, Germany). Moreover, heart rates of the boys were monitored during the GXT by telemetry (Polar Heart Rate Transmitter Model T34, Germany). The boys were asked to avoid heavy physical activities 24 hours before the GXT. VO2peak was calculated as the greatest breath-by-breath VO during 20 consecutive seconds. To confirm that boys attained their VO2peak, at least 2 of the following 3 criteria were met: 1) respiratory exchange ratio was >1.10, 2) maximal HR was not less than 90% of the age-predicted maximal HR (208-0.7 × ages) (19), and 3) the subject was exhausted and refused to continue despite the verbal encouragement (20).

Six-minute walk test

The 6MWT was performed on 30-meter long corridors of selected schools according to the American-Thoracic Society guidelines (4). All participants were instructed to walk back and forth in a straight line as fast as possible, self-paced over a 6-minute period of time. During the walk, subjects were given standardized phrases and informed of the time elapsed every 1 minute. Heart rates of the subjects were measured during the 6MWT by telemetry (Polar Heart Rate Transmitter Model T34, Germany). At the end of the 6MWT, the total distance covered in 6-minute walking was recorded as 6MWD. In order to eliminate the bias of the 6MWT, all the 6MWT measurements were performed by one examiner. Validity and reproducibility of the 6MWT has been confirmed in our previous study (R=0.638, intra-class correlation coefficient, ICC=97) in Iranian healthy children and adolescent boys (12).

Statistical analyses

We used the rule of 20 events per variable (EPV ≥20) to determine acceptable sample size (21). Based on previous literature, five independent variables which were readily obtained (i.e. age, weight, height, BMI, and HR) were related to VO2peak n (12-18). Hence, the minimal sample size was 100 subjects to eliminate bias in regression coefficients. Of course, to eliminate bias in regression

coefficients and increase the accuracy of the prediction models, we selected more subjects (n=157).

Pearson's product correlations were calculated between the independent variables (age, height, weight, BMI, resting heart rate, and 6MWD) and objectively measured VO2peak. Stepwise regression analysis was used to generate the VO2peak prediction equations. Suitability and precision of the regression equation were evaluated using multiple R^2, the absolute SEE, and relative SEE (%SEE). Since the efficiency of multivariate regression analysis highly depends on correlation structure between predictive variables, in order to control the biased estimation of the estimation models, collinearity of the VO2peak estimation models were controlled by Durbin-Watson test, variance inflation factor, and Tolerance indices (22). The prediction model obtained from the prediction group was then cross-validated in the present subjects using the Bland-Altman plot and Pearson correlation (22). Measured and predicted VO2peak values were compared using paired Student's *t* test and Pearson correlation between these values. All analyses were performed using SPSS software, version 24.0 and alpha level was set at $P < 0.05$.

Results

Descriptive data for the GXT, 6MWT, and anthropometric variables are presented in Table 1. The mean VO2peak and 6MWD were 41.80±6.67 mL/kg/min and 747±58 m respectively. The boys performed the 6MWT with the intensity of 85% of their measured maximal heart rate. Correlations of independent variables with VO2peak are presented in Table 2. These correlations were statistically significant (R = 0.318-0.853, $P < 0.001$). Furthermore, a stronger partial correlation adjusted for age was observed between VO2peak and independent variables (Table 2).

The results of the stepwise multiple regressions are presented in Table 3. Based on standardized regression weights (β), 6MWD explained the considerable amount

Table 1. Characteristic of participants (n= 157)

Variable	Mean±SD	Min	Max
Age (y)	14.92±1.35	12.55	17.7
Height (cm)	167.49±9.93	137.40	193.50
Weight (kg)	60.65±16.17	28.11	113.21
BMI (kg/m²)	21.39±4.50	12.44	35.27
RHR (bpm)	79.57±9.65	58	102
VO2max (mL/kg/min)	41.80±6.67	22.10	55.80
VO2LT (mL/kg/min)	26.08±6.32	14.80	41.10
RER	1.24±0.08	1.06	1.50
HR$_{max}$ (bpm)	200.85±7.64	186	221
6MWD (m)	747±58	526	912
6MWT HR (bpm)	172.02±10.73	148	193

BMI: Body mass index, VO2max: maximum oxygen uptake, 6MWD: 6-minute walk distance, HRmax: measured maximal heart rate, 6MWT HR: heart rate at end of the 6MWT, RER: respiratory exchange ratio, RHR: resting heart rate. R: correlation coefficient.

Table 2. Correlation of VO2max With Independent Variables (n= 157)

Variable	R
Weight (kg)	-0.539*
BMI (kg/m²)	-0.705*
RHR (bpm)	-0.318*
6MWD (m)	0.853*

BMI: Body mass index, VO2max: maximum oxygen uptake, 6MWD: 6-minute walk distance, RHR: resting heart rate. R: correlation coefficient, *$P < 0.001$.

of variance in VO2peak. VO2peak estimation model-1 showed that 6MWD could explain 73% of the VO2peak (mL.kg^{-1}.min^{-1}) variance in Iranian adolescent boys (R^2= 0.728, SEE= 3.488 mL.kg^{-1}.min^{-1}, $P < 0.001$) according to the following equation: VO2peak (mL.kg^{-1}.min^{-1}) = -30.85 + (0.097 × 6MWD). The multiple regression model-2 showed that 6MWD and BMI could explain 83% of the VO2peak (mL.kg^{-1}.min^{-1}) variance in Iranian adolescent boys (R^2 = 0.825 SEE = 2.81 mL.kg^{-1}.min^{-1}, $P < 0.001$) according to the following equation: VO2peak (mL.kg^{-1}.min^{-1}) = -3.518 + (0.076 × 6MWD$_m$) – (0.537 × BMI$_{kg/m2}$) (Table 3).

A slight difference was found between the measured and predicted VO2peaks (41.80 ± 6.67 and 41.77 ± 6.05 mL/kg/min, respectively, P=0.955) (Figure 1). While, a strong correlation (R=0.908, $P < 0.001$) was observed between the measured and predicted VO2peaks in the subjects (Figure 2). The Bland-Altman plot (Figure 3) illustrates the strong agreement between the two values. The mean difference (95% CI) between the measured and predicted VO2peaks observed in the subjects under this study was 0.013 (-5.577-5.603 mL/kg/min).

Discussion

This study was the first attempt to develop VO2peak prediction formula using 6MWT in Iranian healthy adolescent boys. A strong correlation was found between 6MWD and directly measured VO2peak obtained during GXT. The proposed model could be able to predict VO2peak of the adolescent boys by 6MWD and BMI with a satisfactory accuracy (R^2= 0.825, SEE= 2.81 mL.kg^{-1}.min^{-1}, $P < 0.001$).

Maximal exercise testing is perhaps the most challenging issue in all physical fitness assessment tests, not only for the client but also for the technician(s). However, applicability of this standard method in large scale is limited (2). Many attempts have been made to develop field exercise prediction models for estimation of aerobic capacity. Several studies have demonstrated that the moderate intensity exercise tests were useful in predicting VO2peak variance (13,14,17,18). Since the 6MWT is a sub-maximal, short, easily administered field exercise test and does not require expensive and sophisticated equipment, this test was preferred to other complex and hardly-conducted laboratory standard tests (3,23).

Distance covered during 6MWT is commonly used

Table 3. Multiple regression analysis of VO2max (dependent variable) and 6MWD and BMI (independent variables) (n=157)

Prediction model	Coefficients	β	SEE (mL/kg/min)	SEE%	R^2
Model 1[*]			3.488	8.3%	0.728
Constant	-30.85				
6MWD (m)	0.097	-0.853[*]			
Model 2[*]			2.81	6.7%	0.825
Constant	-3.518				
6MWD (m)	0.076	0.667[*]			
BMI (kg/m²)	- 0.537	-0.363[*]			

VO2max: maximum oxygen uptake, BMI: body mass index, 6MWD: 6-minute walk distance (m), β: standardized regression weights, SEE: Standard error of the estimation, SEE% = SEE/mean of measured value × 100 as partial SEE, R^2: coefficient of determination, [*]$P<0.001$.
Model 1: VO2max (mL/kg/min) = -30.85 + (0.097 × $6MWD_m$)
Model 2: VO2max (mL/kg/min) = -3.518 + (0.076 × $6MWD_m$) – (0.537 × $BMI_{kg/m2}$)

to assess functional capacity of healthy children and adolescents. Only a very few studies have so far compared the 6MWT with direct measurement of the VO2peak in healthy adolescents (5,12). Our study confirmed this previous result using a more powerful sample size to such a degree that strong correlation was found between 6MWD and VO2peak (r=0.853). To our knowledge, no previous study has attempted to develop a prediction model to estimate VO2peak using 6MWT in healthy adolescent boys. However some studies have developed prediction models based on the 6MWT in adults (14,17,18,) as 6MWD and anthropometric indices could predict aerobic capacity.

In the present study, independent variables were independently related to the VO2peak (Table 2). A number

of studies have documented the relationship between anthropometry variables and VO2peak in healthy children and adolescents (24). The correlation between VO2peak and 6MWD has been reported in healthy children and adolescents (R=0.44-0.723) (5,12), obese children (r=0.34) (7), and in children with cystic fibrosis, cardiorespiratory disease, and severe illnesses (r=0.70–0.76) (13,24-26). Differences between the subjects in these studies (healthy vs. sick) may explain the inconsistent results. According to the studies, the most important variables affecting VO2peak are weight and BMI (27,28).

Previously published CRF estimation models from field exercise tests reported varied R and SEE values, ranging from 0.42 to 0.91 and 2.05 to 4.57, respectively (1, 3). In the present study, R^2 and SEE values determined by the regression model-1 (R^2 = 0.728, SEE= 3.488 mL/kg/min ∼8.34% of the mean VO2peak, $P<0.001$, $P<0.001$) and model-2 (R^2= 0.825, SEE= 2.81 mL/kg/min ∼ 6.76% of the mean VO2peak, $P<0.001$, $P<0.001$) were well and satisfactory (Table 3). In the current study, BMI could explain 73% of VO2peak of the adolescents according to VO2peak prediction modle-1. Furthermore, BMI and 6MWD could explain 83% of VO2peak of the adolescents according to VO2peak prediction modle-2.
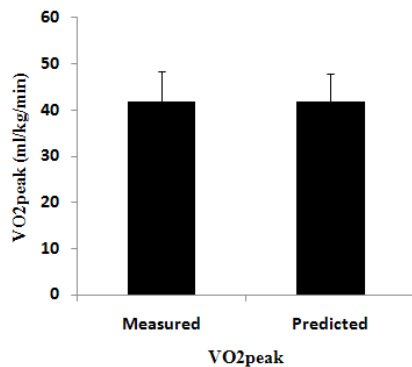

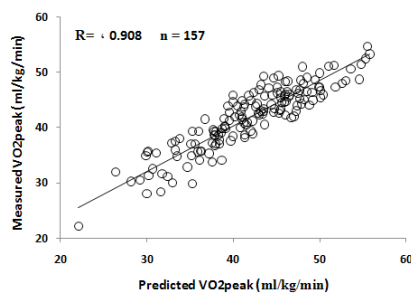**Figure 1.** Difference between measured and predicted VO2peaks (P=0.955).

Figure 2. Correlation between measured and predicted VO2peaks.
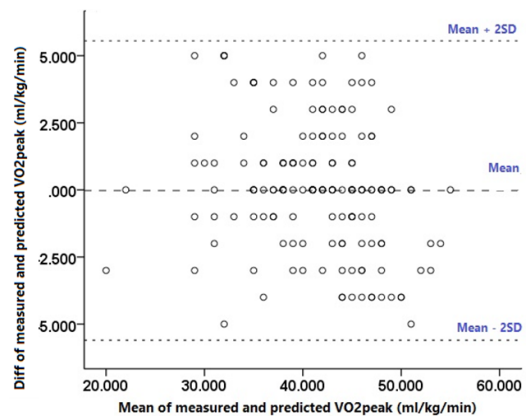

Figure 3. Bland-Altman plot of agreement between measured and predicted VO2peaks. The bias (mean difference between the two paired means) was 0.013 mL/kg/min (- - - - -) and the limit of agreement (…….) was between -5.57 and 5.60 mL/kg/min.

Based on the results of this study, adding BMI to the VO2peak prediction equation improved the accuracy of equation, in such a way that R^2 value was increased and SEE value was decreased (Table 3). It was confirmed that when multiple predictors were used, the criterion-related validity was significantly higher than the only performance score (only time, distance, or heart rate). Therefore, apart from the waking performance score, adding other individuals' variables such as body composition may significantly improve the estimation of the VO2peak (3). Differences in R^2 and SEE values may contribute to the sample size, age range, type and number of predictor variables, and differences in the ethnicity of the subjects (5-12). Whereas we assumed the onset of puberty in boys at the age of 13, we allocated a large number of subjects to the ages of 13 and 14 to decrease modification effects of the puberty. It seems that this strategy improves the accuracy of 6MWD and VO2peak prediction model (22).

We investigated the stability and performance of proposed prediction model-2 using the Pearson's product correlation value (R) and Bland-Altman plot in the adolescent boys. Considering the high R value (R=0.908, $P<0.001$) (Figure 2), slight differences between mean measured and predicted VO2peak values (41.80±6.67 and 41.77±6.05 mL/kg/min, P=0.955 respectively) (Figure 1), and high agreement between two measures (Figure 3) (29), the performance of the VO2peak prediction model-2 in adolescent boys is supported. However, in order to generalize our VO2peak prediction equation to the Iranian population, it is necessary to evaluate the efficiency of the VO2peak prediction model-2 in Iranian healthy adolescents. The validity of this native VO2peak prediction equation is also necessary for application in patient populations.

Considering the importance of cardiorespiratory system efficiency in quality of life (30), as well as the unwillingness of people to perform maximal GXT (31), the importance of the native VO2peak prediction equation based on submaximal 6MWT in Iranian population is highlighted.

Strengths and Limitations

This study was an original investigation, since, to the best of our knowledge, no study has demonstrated that 6MWT would predict the aerobic capacity of healthy adolescents. The relatively large sample size (n=157) with varied body composition and VO2peak values of the healthy boys helped support the generalizability of the prediction model-2 to the healthy adolescents. Direct measurement of VO2peak of the boys during GXT by treadmill was remarkable. In addition, since each of the predictor variables were easily obtained, it is believed that VO2peak estimation model-2 based on 6MWT and anthropometric measures may be a routine component of CRF examination in different settings (i.e. physical education classes, gymnasiums, and exercise therapy). Furthermore, it could be utilized for the evaluation of CRF in large epidemiological cohorts.

Conclusion

Exercise and fitness instructors, physicians, and physiotherapists could be able to accurately assess the level of readiness of the cardiorespiratory system by utilization of a simple, safe and inexpensive native VO2peak prediction equation based on the 6MWT in adolescents. It seems that this native VO2peak estimation equation could be useful in assessing the effect of clinical and sports prescription on cardiopulmonary function. This requires further investigations.

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