

An Equation for the Prediction of Oxygen Consumption in Chinese Adults

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Abstract: To develop and validate a reference equation (RE) for prediction of VO_{2peak} in Chinese adults and compare the equation cited by Wasserman, Edvardsen, Nevil and Itoh. we reviewed the data of 554 adults with treadmill Bruce protocol of CPET (breath by breath) from R+ clinic in Chengdu. Ultimately, 313 adults (aged from 20-59 years) including smokers, obese, were judged to have normal cardiorespiratory system without vascular disease (CVD), hypertension, diabetes and other chronic pulmonary disease based on case history, physical, electrocardiogram during rest and exercise, and exercise performance. The 313 sample was divided into 80% construction group (CG) and 20% validation group (VG) using a case random method. Oxygen consumption, Maximal heart rate (HRmax) and respiratory exchange ratio (RER) were collected in the state of exhaustion. The influence of potential confounding factors, such as age, sex, weight, height and BMI were analyzed for their influencing power at the RE. The equation was predicted by regression analyses. RE was also tested in the VG. Simultaneously, we compared measure VO_{2peak} with predicted values calculated with four equations from Wasserman, Edvardsen, Nevil and Itoh. The line chart that predicted VO_{2max} changes in BMI, height classification and measured among equations was plotted. The mean age and VO_{2max} were 36.63 ± 9.49 years and 32.82 ± 6.01 ml.kg⁻¹.min⁻¹, respectively. For model construction, two prediction equations with acceptable accuracy were developed ($R^2 = 0.67 - 0.71$; SEE = 0.02028 - 0.02033). In VG, the difference was not significant between measured and predicted VO_{2peak} from model 2 and model 1 ($P > 0.05$). However, difference came up between the average VO_{2peak} predicted by cited equation and the CPET measured VO_{2peak} , as well as the difference gotten from the RE ($P < 0.001$). RE presents VO_{2max} values close to those directly measured by CPET, while Europe and America equations overestimated the VO_{2max} . The predicted values of VO_{2max} calculated from Itoh equation revealed a very good consistence among normal and low weight.

Keywords: VO_{2peak} , Equation, Chinese Adults

1. Introduction

Cardiorespiratory fitness (CRF) is an independent risk predictor or prognosis of health and various diseases [1], that can be directly measured as maximum oxygen consumption (VO_{2max} or VO_{2peak}) from CPET. Indeed, CPET is a widely applied routine procedure in daily clinical work in European and American countries. However, as a new idea of medical and health, CPET is not put into practice widely without

enough consciousness during the last decade, since being introduced in China. Primitive fitness assessment methods, such as step test or 6-min walk test are often used to estimate CRF in most exercise and cardiac rehabilitation institution, but only to qualitatively evaluate, that cannot direct the rehabilitation program and clinical treatment effect accurately. Only a few hospitals develop CPET for heart failure and

chronic lung disease to promote the function recovery of cardiopulmonary.

Many epidemiologic studies have reported that low CRF is associate with 2 to 5 folds increases in cardiovascular disease (CVD) and all-cause mortality [2-4]. Low CRF typically defined as the lowest quartile or quintile on an exercise test, is essential to have accurate reference values to know what constitutes a "normal" value, but a consensus has not been reached on the definition of normal reference values. Commonly, VO_{2max} as the most important index of CRF is usually estimated with sex, age, and in some case, body mass, height and physical activity, by several investigators [5, 6, 7]. Currently, the most widely used Equations published provide reference values using CPET in Norwegian, American and Brazilian population.

For the prediction or estimation equation, it is important to understand the structural and local characteristics of the population for which the equation is created or validated; such equations are created with the goal of obtaining a VO_{2peak} value closest to the actual oxygen consumption [8, 9]. But in China the equation predicting VO_{2max} use in CPET software have not been validated.

The VO_{2peak} values measured directly with CPET can be compared with the VO_{2peak} values predicted for a particular age group [8]. Of note is that the prediction of VO_{2peak} for normality is commonly performed using equations that are not validated for the Chinese population.

Therefore, the present study aimed to construct and validate an equation derived from the Chinese population in Chengdu to predict VO_{2peak} and to compare this equation with the equation of Wasserman, Edvardsen, Itoh and Nevil.

2. Methods

2.1. Study Sample

This study was approved by the Ethics committees of the medical of Sichuan University; West China hospital, Si Chuan, China (administration number: ChiECRCT 20200033).

A total of 554 adult tester, most of them are long-term resident in the cities of Chengdu. These individuals volunteered to R+ clinic for CPET in the city of Chengdu between October 2016 and March 2019.

All volunteers were evaluated by case history and self-report, blood glucose and blood pressure measurement on-site. We include people with age 20-59 years, a maximal exercise test performed on a treadmill and agree to sign a consent form of CPET. To ensure accuracy of the study, we exclusion people with cardiac disease, pulmonary disease and other chronic disease (diabetes, hypertension) or orthopedic disease in the joints of lower limb as these could interfere with physical activity, a peak RER < 1.00, Borg scale rating < 7, and a measurement HRmax < 80% predict HR-max.

Due to the exclusion criteria and invalid measures, 241 participants (i.e., repeat tester = 159, Percutaneous coronary intervention = 2, diabetes mellite = 16, Hypertension = 16, Cancer = 7, pulmonary disease and chronic pain = 31, invalid VO_{2max} measure = 3, Abnormal electrocardiogram and increased blood pressure tester = 4) were excluded from analyses. This resulted in a final dataset consisting of 313 adults. The screening flow-chart is shown in Figure 1.

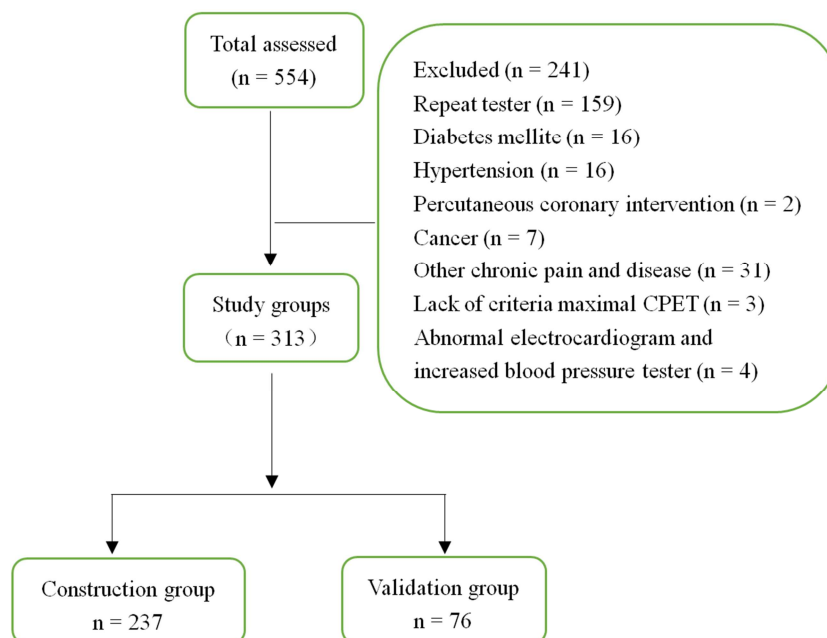


Figure 1. Flowchart for study population selection.

2.2. Cardiopulmonary Exercise Test

A maximal symptom-limited incremental exercise test was

performed using an electrically treadmill of Bruce protocol (track-master TMX 428 Treadmill; California, American) following recommendation VO_{2max} was measured using a

breath-by-breath (COSMED Quark CPET; Italy), and data were analyzed using OMINIA version 1.5.

All examinations were performed in room, environment air and degree according to current guidelines for exercise testing [10-11]. Considering the VO_{2peak} plateau not be achieved by all subjects [12], we used the VO_{2peak} throughout the study. The participant's condition was continuously monitored during the maximal-graded exercise test by perceived exertion (modified Borg scale, RPE 10-scale) oxygen saturation and cuff sphygmomanometer and electrocardiograph (ECG) equipment. A standard 12-lead ECG was obtained at rest, at every minute during exercise and ≥ 3 min during recovery; blood pressure was measured with a standard cuff sphygmomanometer. VO_2 , VE and V_{CO_2} were acquired on a breath-by-breath basis and averaged over 10s intervals. VO_{2peak} was defined as the highest 20-30s average of VO_2 in the last 30s of exercise. The exercise test was considered maximal if it was symptom-limited with overall fatigue (Borg scale rating 9-10) [13]. Participants were considered exhausted from maximal exercise when they met following two criteria: RPE ≥ 7 and a change in respiratory ratio (CO_2/O_2) of at least 1.05 [5].

2.3. Equation Comparison

We compared the RE with the Japanese equation derived from Itoh, Norway equation from Edvardsen, American equation from Wasserman and Nevil which are the classic or the large used standards for directly measuring VO_{2max} .

The Itoh equation that was for ergometer was modified for treadmill as follows: VO_{2max} predicted for male subjects = $0.9 \times \text{weight} \times (0.0521 - 0.00038 \times \text{age}) \times 1.11$, VO_{2max} predicted for female Subjects = $0.9 \times \text{weight} \times (0.0404 - 0.00023 \times \text{age}) \times 1.11$ [14].

Wasserman Karlman equation for the prediction of VO_{2max} was modified for treadmill in men = $[0.0337 \times \text{height} - 0.000165 \times \text{age} \times \text{height} - 1.963 + 0.014/0.006 \times \text{weight}] \times 1.11$; prediction of VO_{2max} in women = $[0.001 \times \text{height} \times (14.783 - 0.11 \times \text{age}) + 0.006 \times \text{weight}] \times 1.11$, where weight in Kg, actual or normalized if overweight or below normal weight [8].

The Nevil [16] equation for the treadmill was as follow: VO_{2max} predicted: $\ln(VO_{2max}) = -0.854 \times \ln(M) + 1.44 \times \ln(H) + 0.424 - 0.346 \times \text{sex} - 0.011 \times \text{age}$, where sex is entered as a [0,1] indicator variable (male = 0 and female = 1).

Edvardsen [15] for the treadmill prediction of VO_{2max} in men = $4.97 - 0.033 \times \text{age}$; prediction of VO_{2max} in women = $3.31 - 0.022 \times \text{age}$.

For the building of equation, we firstly used rectangular scatter plot and curve fit to test the interaction relationship between gender, height, weight, age, BMI and VO_{2max} ; Secondly, Correlation analysis was performed in each other; Last analysis of variance and estimation of regression were applied using stepwise method and nonlinear regression. The P and R^2 was calculated for each factor to determine the correlation and importance, sequence, and percentage of participation for each variable in the construction of the models for prediction of VO_{2peak} . Multivariate and nonlinear regression model was used as follows: $Y = b_0 + b_1x_1 + b_2x_2 + b_3x_3 + b_4x_4 + \epsilon$, $\ln(Y) = b_0 + b_1x_1^{\wedge 3} + b_2\ln(x_2) + b_3\ln(x_3) + b_4x_4 + \epsilon$, for the independent variable of gender, height, weight and age.

3. Statistical Analyses

SPSS (version 22.0) statistical software was used for analyses. Continuous variables were represented as mean \pm standard deviation, and categorical data are represented as percentages. This method applied the criteria to include variables with a significance of $\leq 5\%$ in the F-test and to exclude variables with a significance of 10% from the regression and R of each variable. For equation construction, a multivariate regression model and curve estimated was used. The correlation was calculated using the intraclass correlation coefficient (ICC). For comparisons between equations, the Student's paired t-test and Wilcoxon test were used. The distribution of positive and negative equation residues was represented as absolute values and percentages. The residues of the regression of VO_{2max} indicated a normal distribution curve using the Shapiro-wilk test. Internal validation was evaluated using Cronbach's alpha. All tests with a $P < 0.05$ were considered statistically significant.

4. Results

4.1. Selection of the Reference Population

Relevant characteristics and distributions of all studies are shown in table 1.

Table 1. General profile of the group subjects.

Characteristics	Mean \pm SD (Min/max)		
	Total	Construction group	Testing group
Sample (n)	313	237	76
Female (n or %)	122 (38.98)	92 (38.82)	30 (39.47)
Age (Years)	36.63 \pm 9.49 (20, 59)	37.02 \pm 9.55 (21, 59)	35.42 \pm 9.27 (20, 57)
Height (cm)	168.42 \pm 7.61 (152, 186)	168.06 \pm 7.58 (154, 185)	169.54 \pm 7.64 (152, 186)
Weight (Kg)	66.68 \pm 12.51 (44, 117)	66.46 \pm 12.41 (44, 117)	67.36 \pm 12.88 (44, 101.6)
BMI (Kg/cm ²)	23.37 \pm 3.19 (16.4, 34.2)	23.39 \pm 3.14 (16.8, 31.6)	23.32 \pm 3.38 (16.4, 34.2)
VO_{2max} (L.min ⁻¹)	2.19 \pm 0.55 (1.09, 3.74)	2.16 \pm 0.55 (1.09, 3.71)	2.26 \pm 0.57 (1.13, 3.74)
RER	1.30 \pm 0.12 (1, 1.78)	1.30 \pm 0.12 (1, 1.78)	1.31 \pm 0.127 (1.02, 1.61)
HRmax	179.21 \pm 12.66 (134, 207)	179.21 \pm 12.74 (134, 207)	179.22 \pm 12.47 (147, 205)

Data are presented as n (%), n or mean \pm SD, unless otherwise stated, BMI: body mass index.

Development of a VO_{2peak} prediction equation.

4.2. VO_{2peak} and Relevant Factors

In the study, all variables for pairwise correlation were examined, and table 2 shows the correlation coefficient, such as P and R. Table 2 shows the degree of VO_{2peak} correction was sex ($R=0.734$), Height ($R = 0.731$), Weight ($R = 0.685$), Age (man $R= -0.379$, woman $R = -0.225$), and all variables were significant predictors. The highest correlation was between the measured VO_{2peak} and Sex, and the lowest between the measured VO_{2peak} and age. The best relationship between height, weight and VO_{2max} is power function, while between age and VO_{2max} is cubic power, follow by linear.

Table 2. All variables for pairwise correlation.

Variables	VO_{2peak}	Sex	Age	Height	Weight	BMI
VO_{2peak}	1	-	-	-	-	-
Sex	0.734**	1	-	-	-	-
Age	-0.09		1	-	-	-
male	-0.379**	0.171**		-	-	-
female	-0.225**			-	-	-
Height	0.721**	0.707**	-0.077	1	-	-
Weight	0.685**	0.655**	0.167**	0.716	1	-
BMI	0.467**	0.444**	0.285**	0.325**	0.890**	1

**Coefficient is significant ($P < 0.001$).

Model 1 included prediction variables (i.e., sex, age, weight and height) was applied to Linear regression analyses using stepwise method. All variables in the model were significant predictors of VO_{2max} . Model 1 was the optimum goodness of fit linear equation with $R^2 = 0.67$, VO_{2peak} ($L \cdot min^{-1}$) = $-1.462 + 0.501 \times S + 0.015 \times H + 0.011 \times W - 0.012 \times Age$ (Sex male = 2, female = 1, $R^2 = 0.67$, $P < 0.001$).

Model 2 was a Nonlinear equation: $LN(VO_{2max}) = 0.248 \times sex + 1.09 \times LN(height) + 0.347 \times LN(weight) - 1.163 \times 10^{-6} \times age^3 - 6.624$ (Sex male = 2, female = 1, $R^2 = 0.71$, $P < 0.001$). For the two VO_{2max} prediction models, there was

no multicollinearity among the predictor variables (VIF ranged from 1.01 to 3.40; desirable $VIF \leq 10$, or parameter correlation estimate < 1). However, the regular pattern and shape were found in the scatter plot between predicted VO_{2max} and residuals and The Shapiro-Wilk test indicated that residual was not normally distributed ($P < 0.05$) in linear equation, but not in nonlinear equation ($P = 0.076$). Therefore, the nonlinear equation was chosen as the best model 2 due to its accuracy.

4.3. Cross-validation of the Chosen VO_{2max} /Peak Prediction Models

Compared the basic information include age, sex, height, BMI and weight, there is no significant difference between the CG and VG (table 1).

The VO_{2peak} prediction models and quoted equations from Japan, Canada, America and Norway were compared to the measured VO_{2peak} value using the validation group dataset. All quoted equations were constructed based on treadmill except the Itoh and Wasserman equation derived from cycle ergometer.

The differences between measured and predicted VO_{2peak} among the two model equation were not significant ($P > 0.05$). However, there was a significant difference with predicted VO_{2peak} using the cited equations from Itoh, Nevil, Wasserman and Edvardsen ($P < 0.001$) in VG and CG (Table 3). Intraclass correlation analysis reveal R value between the measured VO_{2peak} and equations in VG and CG as follows, model 2 ($R = 0.90$, CI:0.84-0.94), ($R = 0.89$, CI:0.86-0.916), Itoh ($R = 0.915$, CI:0.866-0.946), ($R = 0.666$, CI: 0.569-0.741), FRIEND ($R = 0.880$, CI: 0.811-0.924) ($R = 0.880$, CI: 0.845- 0.907) and Edvardsen ($R = 0.860$, CI:0.778-0.911) ($R = 0.858$, CI:0.816-0.890) and Wasserman ($R = 0.903$, CI:0.847-0.938) ($R = 0.894$, CI:0.863-0.918). Although all the cited equations show a very good correlation with measured VO_{2peak} , Z test reveals a significant difference in VG and CG (table 3).

Table 3. Statistical values of the equations in CG and VG.

	Statistical	Measured	RE	Wasserman	Itoh	Nevil	Edvardsen
construction	Mean	2.16	2.15	2.97	2.52	1.74	3.75
	Min	1.09	1.21	1.92	1.5	1.11	3.02
	Max	3.71	3.12	3.93	4.29	2.59	4.28
	SD	0.55	0.45	0.39	0.51	0.31	0.32
	ESE	-	0.020	0.023	0.032	0.026	0.027
	T/Z		-0.14b	-11.68c	10.46c	-12.52c	-13.34b
	P		0.891	0.000	0.000	0.000	0.000
validation	Mean	2.26	2.20	2.63	2.43	2.77	3.29
	Min	1.13	1.38	1.54	1.49	1.56	2.12
	Max	3.74	3	3.72	3.98	3.85	4.24
	SD	0.57	0.43	0.64	0.59	0.63	0.61
	ESE	-	0.035	0.041	0.037	0.045	0.048
	T/Z		-1.21c	-6.482b	4.095c	-7.145b	-7.575c
	P		0.23	0.0000	0.0000	0.000	0.0000

c: negative; b: positive.

Values from measured equations over wide ranges of height, BMI, and age are compared with reference and cited equations for VO_{2peak} published by Wasserman et al, Itoh et al, Nevill et al and Edvardsen et al in Figure 2 (man) and Figure 3 (women).

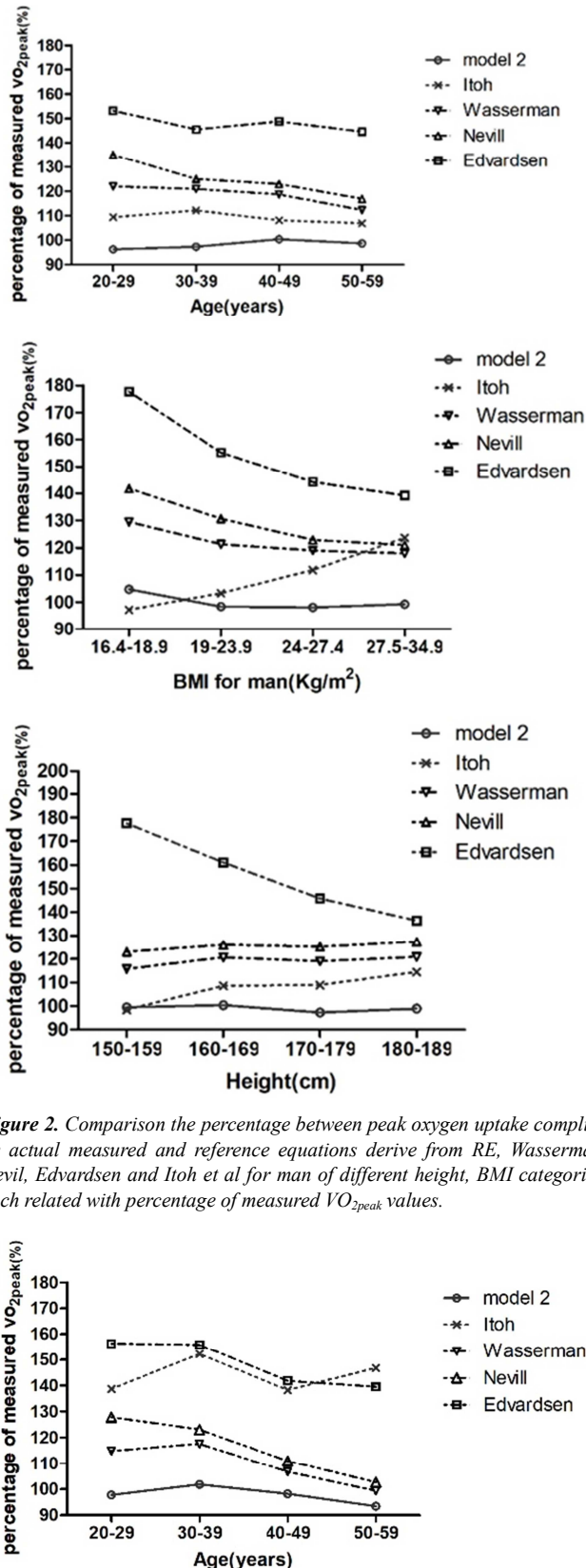


Figure 2. Comparison the percentage between peak oxygen uptake complied by actual measured and reference equations derive from RE, Wasserman, Nevill, Edvardsen and Itoh et al for man of different height, BMI categories, each related with percentage of measured VO_{2peak} values.

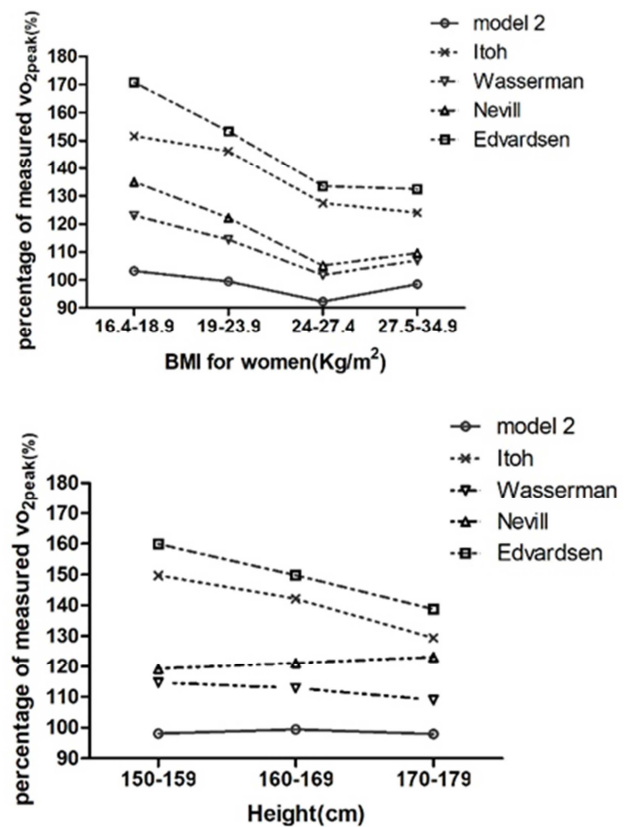


Figure 3. Comparison the percentage between peak oxygen uptake complied by actual measured and reference equations derive from RE, Wasserman, Nevill, Edvardsen and Itoh et al for woman of different height, BMI categories, each related with percentage of measured VO_{2peak} values.

5. Discussion

This review study constructs a VO_{2peak} predicted equation according to the actual measured values for the interpretation of CPET and several parameters derived from 237 sample apparently disease-free adults aged 20 to 59 years from Chengdu in China. The RE incorporated several variables, including sex, age and body composition, and be able to predict VO_{2peak} with a great accuracy compared with VO_{2peak} measured by CPET. RE was developed from a sample with height from 152cm to 186cm and weight from 44kg to 101kg and BMI from 16.8 kg/m² to 31.6 kg/m², in which BMI ≥ 24 kg/m², were 42.19%. In addition, $RER \geq 1$ or a Borg score of ≥ 7 as the end criterion chosen for an acceptable VO_{2peak} was selected in total sample of 554. According as case history, self-report, blood glucose and blood pressure measurement on-site, we excluded chronic pain and disease. These methods may decline the likelihood of underestimating or overestimating the VO_{2peak} . VO_{2peak} is challenging mainly by genetic differences, ethnicity, body composition, and physical activity levels of a particular population may differ from the population in which the equation was initially tested [8, 17, 18]. Both the prediction and estimation equations may overestimate the actual oxygen consumption. For this reason, the distinction between the prediction and estimation

equations for the calculation of $\text{VO}_{2\text{peak}}$ is necessary. In the prediction equation, $\text{VO}_{2\text{peak}}$ is dependent on pretest physical characteristics, including age, gender, body composition, and physical activity level. Bruce *et al* [18] evaluate the correlation between $\text{VO}_{2\text{peak}}$ and gender, age, physical, weight, height, smoking measured by treadmill revealed that gender and age were the most important factors follow by physical activity, weight and height to affect the predicted $\text{VO}_{2\text{peak}}$ on 295 normal subjects using stepwise multiple regression analysis.

In the present study, the important of variables, in descending order, was as follows sex, height, age, weight. This difference in the results may be due to two factors; the first factors is corrected with subject physical activity who haven't the regular exercise habits that defined didn't exercise 3-6 days a week over 3 months and light work activities. Another factor is related to sample age range, in which a wider age cohort include child, youth and elderly people may have a higher age correlation [15, 19].

The average $\text{VO}_{2\text{max}}$ obtained by Itoh equation, Wasserman, Edvardsen and Nevil are 107%, 116%, 123%, 146 higher than the measured value. Although the Cronbach's alpha is high, the accuracy displayed a significant difference. The equations from Edvardsen *et al* [15] involving predominantly active subjects, whose height and weight levels were significantly higher and had a wider age range than our study population. These differences lead to an overestimated $\text{VO}_{2\text{max}}$ of our subjects. Moreover, this difference may be related to the higher active stature and to genetic factors in the Norwegian population. Another Norwegian study by Aspenets *et al* [20] include 4631 individuals in which 90% were active or athletes revealed more higher $\text{VO}_{2\text{max}}$, therefore, the predicted $\text{VO}_{2\text{peak}}$ obtained from athletes, physical trainers, military personnel, or organized sports team participants are higher and cannot represent the reference value of the general population [21, 22]. An American FRIEND study involved a large number of 7783 subjects aged 20 - 79 training on a treadmill obtained the $\text{VO}_{2\text{peak}}$ values of $40.8 \text{ mL kg}^{-1} \text{ min}^{-1}$ and $30.15 \text{ mL kg}^{-1} \text{ min}^{-1}$ for men and women aged 20 - 59 years respectively [16]. These values were 19% and 3% higher than those obtained for man and women in the present study. Another equation from Wasserman in the United States also overestimates the $\text{VO}_{2\text{max}}$ overall, but its predicted value is the closest to the actual measured values. The Japanese equation, which derived from an Asian group, showed a very consistence and accuracy with the average of measured $\text{VO}_{2\text{max}}$ for men with a BMI < 24 kg.m^{-2} and height < 170 cm, but overestimated in overweight, obesity, height > 170 cm and as well as the effect gotten in a women group. Regardless of weight and height, the quoted equations overestimated the $\text{VO}_{2\text{max}}$ in adults at the age of 20 - 59 years, and the predicted values from the Japanese equation is closest to the measured $\text{VO}_{2\text{max}}$ at the age of 40 - 59 years, that may be related to the overall characteristics of the sample. Due to the similar body size in height, weight and genetic, the average of predicted $\text{VO}_{2\text{max}}$ calculated by Itoh equation performed a good agreement in certain characteristic populations. However, the equations of Itoh and Wasserman derived from subjects training on a cycle ergometer corrected

by the factor 1.11 for the treadmill, that may have contributed to the increased prediction error.

6. Conclusions

The equation of this study derived from the Chinese adults was able to predicted $\text{VO}_{2\text{max}}$ and showed a comparable accuracy in the internal validation test. The $\text{VO}_{2\text{max}}$ of Chinese were overestimated by Europe and American equation. This article was the first investigation to reports the data of cardiorespiratory fitness testing from CPET in Chinese adults. Further research will be required to expand the sample to cover different regions and ethnic groups that more accurate for Chinese populations.

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